

THE
EXTRA PHARMACOPŒIA

MARTINDALE
AND
WESTCOTT

VOL. II

NINETEENTH EDITION

REVISED BY

W. H. MARTINDALE

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THE
EXTRA
PHARMACOPŒIA
OF
Martindale and Westcott

REVISED

BY

W. Harrison Martindale, Ph.D., Ph.Ch., F.C.S.

NINETEENTH EDITION.

IN TWO VOLUMES.

VOL. II.

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EXTRA

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113

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VOLUME II.

CONTENTS.

	PAGE
Preface to the Nineteenth Edition	v-xxii
Introduction	xxiii
Abbreviations	xxv-xxx
International (1925) Atomic Weights and Atomic Numbers	xxxi
Isotopes	xxxii, xxxiii
Suggested International Atomic Weights for Pharmaceutical Purposes	xxxiv
The Structure of the Atom	xxxiv, xxxv
Periodic Table of Elements (Mendeleeff)	xxxvi
Poisons Schedule Revisions	xxxvii
Weights and Measures	xxxviii
Analytical Addenda to Materia Medica in Vol. I.	1-163
Supplement	164-169
Animal Organotherapy	169-175
Physiological Standardisation	176
Table of Action of Acids on Metals and their Oxides	177-186
Indicators for use in Volumetric Analysis	187-192
Determination of Hydrogen Ion Concentration of Solutions	190-192
Scheme for the Recognition of Organic Substances used in Therapeutics	192-203
Corroborative Tests	204-247
Melting Points and Consistences of Fats and Waxes	248
Freezing Mixtures	249
Sulphuric, Hydrochloric and Nitric Acid Sp. Gr. and Percentage Tables	249
Potassium and Sodium Hydroxide Solution Sp. Gr. and Percentage Tables	249
Drop Measure Table	250
Synthetic Notes.—Physiological Effect in Comparison with Chemical Constitution of Synthetic Drugs	251-257
Sterilisation	257-261
Antiseptic Powers of Chemicals and Disinfectants	262-278
Iontophoresis	279-291
Radiology	291-322
Ultra-Violet Rays	315-320
Radium	322-350
Radio-active Disintegration Products of Thorium	351-355
Uranium and Uranium 'X'	355-356

	PAGE
Tests and Microscopic Methods for Examining Urine, Blood,	
Fæces, etc. 357-413
Urine 357-391
Blood 391-408
Cerebro-Spinal Fluid408-411
Fæces 411-413
Pleural and Peritoneal Fluids 413
Stomach Contents Examination 413-418
Water Analysis Notes (Chemical) 418-434
Iodine in Natural Waters 422-433
Sterilisation for Army Use 434
Poisoned Water 434
Water Examination, Bacteriological435-447
Mineral Waters 447-458
British Spas and Climatic Health Resorts459-463
Milk Analysis 464-489
Résumé of Acts and Regulations 467-472
Pasteurisation 472-477
Milk Supply and its Consumption 477-478
Veterinary Opinions 478-480
Milk Preservatives 480-482
Survey 482-485
Thermo-Isolated Milk Supply 483-485
Artificial Cream Act 486
Bacteriological Examination 487
Butter Analysis 489-490
Margarine 490
Food and Drugs (Adulteration) Act 1928491-492
Food Preservatives 492-495
Aniline Dyes used in Colouring Foods.. 495-498
Mould Inhibition by Preservatives 498-500
Gas Poisoning 500-502
Carbon Monoxide and Dioxide Tests 501
Ptomaines 502
Bacteriological and Clinical Notes with Reference to Special	
Diseases 503-614
Staining Methods, Culture Media 614-620
Embalming 620-621
Proprietary Medicines 621-637
Stains on Cloth and the Skin, Methods of Removal638
Analyses of Prescriptions 639
Glossaries 640-649
General Index to Vols. I. and II. 650

PREFACE

TO THE EXTRA PHARMACOPŒIA.

EDITION XIX. VOLUME II.

The first volume of this Edition, devoted mainly to treatment with drugs and chemicals, was issued in June, 1928. The second volume is concerned with matters of diagnosis, analysis and assay of *materia medica*, and divers subjects too numerous to include in the main portion of the work. It, like the corresponding volume of the 18th (1925) Edition, is published a year later, after the necessary revision, which involved drastic excision of out-of-date information, and the inclusion of such new matter as we consider important to medical practitioners, pharmacists, analysts, and others.

In spite of our endeavours, the overwhelming bulk and character of the scientific literature to-day has militated against the conciseness which we prefer, and holding, as we do, that the tenets of, say, five years ago, are not necessarily invalid, we sometimes purposely retain the relatively old material, giving references both to it and to the newer and perhaps more fashionable views by which it is being superseded. In instances where the new matter would cause chapters to be overloaded, it has been necessary to refer the reader to previous editions for data that had to be omitted.

ANALYTICAL ADDENDA TO CHEMICALS AND MATERIA MEDICA.

Chemical, Pharmaceutical and Medical Research has been active during the last four years. New pharmacological investigations, processes of treatment, and diagnostic methods have been evolved.

We observe that a Professor of Pharmacology at one of our Universities recently made a plea for increased facilities for instruction in his subject, and in drawing attention to the advances in Chemotherapy made abroad during the last thirty years emphasised that fundamental advances in treatment during that period have originated from animal experiments in association with physiology.

We heartily agree that the science of Pharmacology should be encouraged, but we submit that problems connected with new chemicals for use in man should be approached with caution, as erroneous conclusions, and hence dangerous therapy, may result from deductions from doses suitable for animals, as shown in the Preface to Vol. I.

A large number of the newer remedial agents have not more than a few years of life and popularity, and occasionally we wonder whether the older *materia medica* may not with advantage have their popularity revived, and in some instances be further investigated. We believe that the old and well-tried friends of the general practitioner—‘*Nux*,’ *Belladonna* and their alkaloids, *Digitalis*, *Iodides*, *Bromides*, *Mercurials*, and so on—are prescribed to-day as extensively as ever they were in the past, in spite of the keen competition of modern remedies.

We are inclined to think that many new remedies—including those with vast apparent success—are advocated without sufficient proof of utility. We are of course by no means averse to pharmacological deductions: indeed, the volume under consideration is largely concerned with experimental research in many fields.

We would draw attention to the following features that are new in this volume:—

Æther.—The possible injurious effects of Peroxides and Aldehydes, present as impurities, have attracted attention. Several simple methods of testing are given with our results and with recommendations for storage.

Alcohol, Isopropyl.—Now that this spirit is coming into more general use it is important to know easy methods of detection, and these are available.

Arsenic.—Tests to distinguish the various Organic Arsenicals, and methods of assay, are arranged in a manner handy for reference.

The Medical Research Council’s Report on Biological Standards deals with a modified Toxicity Test for Novarsenobenzol, and details of the test are provided in an abbreviated form. In determining experimental therapeutic activity, spirochetes are to be used in place of trypanosomes—by agreement of the League of Nations Commission on Standardisation of Serums, Serological Reactions and Biological Products.

Certain of the Organic Compounds containing trivalent Arsenic have distinctive chemotherapeutic properties in bacterial infections.

Cannabis Indica.—Its resin, extracts, and tinctures, were included in the Dangerous Drugs Act 1925, which is now in force.

Carbon Tetrachloride.—The latest knowledge in addition to that contained in Vol. I. is to the effect, broadly, that Carbon Tetrachloride cannot be regarded as the ideal anthelmintic. Thymol has replaced it in some parts of the world in the treatment of hookworm.

Cascara.—Notes on cultivation, and on the wood of the tree receive attention on *pp.* 56 and 57.

Digitalis.—The author’s assay process employed in respect of samples of 1929 leaves showed them to be fully up to standard. Physiological methods of standardisation are being improved. The League of Nations Commission on Standardisation, etc., has issued further data on suitable methods, employing an International

Standardised Digitalis Powder. The Ouabain process as used in U.S.X. is recognised as unsound. A number of recent references to the examination of Digitalis and Squill preparations are in this chapter.

Drug Addiction.—All the addenda on this matter are in the Cocaine Chapter. The inclusion of Heroin in *any* proportion—the result of an International Agreement—is referred to.

Resolutions protesting against the Regulations were passed at the 1929 Annual Meeting of the British Medical Association. The restriction was deemed 'oppressive and unnecessary.'

During 1928 a chemist appealed successfully against a conviction for supplying Dangerous Drugs on the prescription of a person who purported to be a doctor but was not: the Appeal was allowed with costs. The magistrate stated that there was nothing to make the chemist suspicious regarding the prescriber's signature.

Ergot.—The Pharmacological Laboratory of the Pharmaceutical Society of Great Britain holds that not an ounce of the Liquid Extract of Ergot, made according to the *B.P.* '14, can be of the slightest medicinal value.

Ferrum.—Some interesting facts relative to 'Food Iron' show that the content in some common foods may range from 0.00015% in lemon juice to 0.019% in parsley.

Indigo-Carmine.—The technique for the use of a solution of this dye in testing kidney permeability is given. Good results are obtained with 5 to 10 Cc. doses intravenously of a saturated solution. Its application in the diagnosis of hydrocephalus is also outlined.

Iodine.—The question of the transmission of Iodine from vegetable foodstuffs to the animal world is now being actively investigated. There amounts to a cycle of intake and elimination. Some of the soils in the cattle-rearing districts have been found poor in the element, whilst in others it is held that the Iodine is being literally 'eaten out' of the ground (*v.p.* 85).

Deficiencies of this nature have to be made good. Whether Iodine deficiency in natural waters, vegetables, and animal foods is directly causative of goitre, especially in children, is a problem that has been discussed for some years. Quite recently the subject has attracted further attention; scientists in many countries have been investigating drinking waters and foodstuffs with a view to its elucidation. If there is a deficiency it can be remedied by the consumption of Iodised Salt in place of the ordinary domestic salt.

An opinion has been expressed that an increase or decrease of Iodine in water does not necessarily indicate a corresponding increase or decrease in soil and foods. We would differ (*v.p.* 431) and anyone conversant with the estimation of the exceedingly minute amounts of Iodine concerned, would agree with us that more accurate data are likely to be obtained from testing water than from the examination of vegetables, etc.

During the past year we have attacked the problem in so far as natural waters in Great Britain are concerned. Waters from

representative districts in different parts of the country have been compared with samples from districts hitherto considered 'goitrous,' and the results of the investigation are given on *pp.* 422-433.

We did not expect any marked differences in Iodine content, nor did we find them. Recent work in New Zealand, which we summarise on *p.* 429, is of great importance in this connection. The New Zealand workers are definitely of the opinion that Iodine deficiency is the essential cause of goitre in that country, as its deficiency in the soil, and thence in foods, is observed in many districts in the islands where goitre is highly prevalent. The deductions go to show that a *diminution in the amount of Iodine may be the causative factor.*

It is of interest that the Iodine content of waters in Finland and in Nebraska, U.S.A., reported on *p.* 431, are much smaller than those in Great Britain, and one would be inclined to class them all as *relatively* goitrous, though the authorities in Finland have been able to make divisions between the small amounts within which they were concerned in that country.

Our research was both laborious and interesting. It was necessary to examine the methods used by workers as early as the '50's up to quite recent times. We do not favour methods involving oxidation and subsequent addition of Iodine, so that by titrating a larger amount of the halogen, more accurate results may be expected. Again, titration with Thiosulphate has a minimum detectable limit. Further, as the amount of Iodine involved is of the order of a few millionths of a gramme per litre (or hundred thousandths of a grain per pint) it is not satisfactory to operate merely upon 2 or 3 litres. Added to which, the fewer chemicals that are introduced in the method the better, as reducing possibility of error.

We evolved a simple procedure. This necessitates evaporating at least 10 litres (preferably 25 or 50) of the specimen and the number of chemicals employed is five only, viz., *Potash, Sodium Nitrite, Hydrochloric Acid, Alcohol and Petroleum Ether* (*v.p.* 424).

An added advantage in this process is that the Iodine extracted is visible as such in solution, and by comparing with freshly made standards the original content is determined. The limit of delicacy is 18 γ , in other words 10 litres of 1.8 γ per litre, but for accuracy a water containing approximately 2 γ per litre should be dealt with by concentrating 25 litres. This assay method is far more delicate than titration, or the Palladium process of Chatin.

Not all the waters mentioned on *p.* 427 have been assayed by our process as the investigation proved too protracted. The figures we give are either those obtained by our own method or by means of Palladium. At a later date we may repeat the analyses made by Chatin's procedure, using the Sodium Nitrite process, in which we have more faith.

An important side-issue of the problem was to ascertain whether Chlorination of water, as now conducted in many parts of the world, results in loss of natural Iodine. The point could only be

settled satisfactorily by comparing the water just prior to Chlorination with it after the treatment.

Supplies of water taken at Hampton, on the Thames, previous to Chlorination at the West Middlesex Water Works, compared with the main supply in West London, gave gratifying results (*v.p.* 429), and we think we may safely say that the town-dweller is not deprived of the Iodine he needs from this source.

We have also examined sea-water in the English Channel on various occasions and by various methods. This presented some difficulties. We believe the content of Iodine is in the neighbourhood of 20 γ per litre.

Bearing on the whole subject it may be mentioned that the germ of wheat contains 15 times as much Iodine as white flour—this goes to feed pigs, as ‘ offals.’

Iodine in Isopropyl Alcohol has advantages over the corresponding Ethyl Alcohol solution as a surgical antiseptic.

Iodinol 40%, an Iodine-Oil addition product, has been employed, by virtue of its opacity to X-rays, for outlining the bronchi and their ramifications. The technique is described. The oral method is preferable. Good diagnostic pictures of the male urethra can also be obtained with the solution and no membranous irritation has been observed.

Iodine.—It is to be regretted that the commercial value of Iodine is kept at an artificial figure. Prices are arranged by the various producers, whether Caliche or Kelp be concerned.

Laminaria extraction is still practised in Scotland, Ireland, France and Japan.

Ipecacuanha.—Emetine poisoning by cumulative effect is a new conception against which we think practitioners treating *E. histolytica* carriers and cases of schistosomiasis should be warned, especially as Emetine in various forms has been given by injection and *per os* for some years, with apparent safety and impunity.

Mercurochrome.—The author provides an assay process for ionised Mercury which is used in his laboratory. The method is simple and shows minute quantities if carried out carefully.

Nutriments.—The food factors necessary for the maintenance of health and body growth are now more clearly stated, according to views expressed in some quite recent papers by leading authorities. The Calorie Values of foods, as a means of conveying minimum standards, had a vogue a few years ago, but was relegated to unpopularity on the arrival of the Vitamin theory. Quite recently it has been considered a deciding factor in the argument as to the relative merits of wholemeal and white bread. It is held that when allowance is made for food calories lost in the fæces, wholemeal bread has a lower calorie value than white bread. Brown bread is considered too irritating for children.

VITAMINS.—An enormous amount of investigation has been conducted in connection with these vital principles. We divide

the chapter on them into General Considerations and Vitamins 'A,' 'B,' 'C,' 'D' and 'E.' The current classification of the Fat-Soluble and Water-Soluble factors on p. 98 is of interest.

We were struck with the opinion that lack of Vitamins results in loss of stability of the nervous system, making for irritability, excitement, fear, anger, and other mental disturbances. It follows, no doubt, that in future the town-dweller who suffers from these defects may be permitted to blame Vitamin deficiencies, *i.e.*, poor foodstuffs, as causative of his shortcomings.

It would be impossible to point to any special statement in the Vitamin Chapter as being the most important. Compressed into nine pages are some eighty abstracts from the recent literature. Divers opinions have been collated, rendering the section up to date, and to these we would refer the reader.

With regard to the Anti-Infective Vitamin 'A', Colour Reactions, both qualitative and quantitative, are surveyed, and we have tried them practically.

For the present it seems safe to assume that materials giving no blue coloration with Antimony Trichloride, even after removal of saponifiable matter, must be devoid of Vitamin 'A' activity. Materials of liver oil origin giving colour reactions characterised by absorption at $610\ \mu\mu$ may be considered active, but those giving reactions characterised by absorption at other positions may be either active or inactive, or mixtures of inactive and active chromogens, and in these biological assay is the only satisfactory method (L. ii./29,220).

'B₁' and 'B₂,' the Antineuritic substance and the Anti-Pellagra body respectively, are considered. Wheat and maize are relatively rich in 'B₁' and poor in 'B₂.'

With regard to 'C', the outstanding point seems to be that its content in milk is diminished by Pasteurising, and, what is of equal note, that diminished heating for a correspondingly *longer* time is more destructive than a high temperature for a *short* period—in other words, the housewife who merely scalds her milk is doing the right thing.

Vitamin 'D.'—This is now well known to be derived from the irradiation of Ergosterol in the skin. Those dwelling in Northern towns suffer from a deficiency of it in winter. Moreover, most of the animal fats they consume are from animals which have received little Ultra-Violet irradiation. Town-dwellers elsewhere also suffer, as the sun's rays cannot penetrate the smoke (*v. p.* 104).

Actinotherapy for rickets, we are told, is rapidly becoming a therapy of the past, in consequence of the discovery of the potency of irradiated Ergosterol. Elsewhere it is claimed that the affection will be a disease of great interest historically, without terrors for the patient or anxiety for the attendant.

Hypervitaminosis, it is said, is only likely to occur from excessive dosage.

The efficacy of this Vitamin in inhibiting the formation of dental caries has been claimed and likewise severely criticised.

Vitamin 'E' is obtainable from Wheat Germ Oil. It is contained in vegetable foods, especially lettuce, and is not destroyed by cooking.

With all this advance in science, we would make one—perhaps gratuitous—observation. We are struck by the anæmic, pinched, unhealthy appearance of many of the dirty, miserably-clad children of the poor in London to-day. Their Vitamin ration must be very short weight. We doubt, in spite of all the vast machinery of supervision and attention which the poor receive, whether any real headway has been made in their health during the last thirty years.

BREAD AND FLOUR.—As already conveyed, the valuable 'offals' in milling, rich in extractive protein, mineral salts, fat, and Iodine are handed on by the miller to the cattle-food vendor, and hence the wheat ear is not used to the greatest advantage of the human consumer.

We have revised the Bread and Flour Chapter, and include many new data (*v.p.* 107 *et seq.*). The 'Yeast' question is dwelt upon. A suggestion is made to use dried Yeast, but we fear its flavour would be objected to by the fastidious consumer.

We again condemn the use of 'Improvers' and Bleaching Agents.

The Departmental Committee on the Use of Chemical Substances in Flour has issued its somewhat belated report. A vast amount of evidence was heard, and we believe the wording of the Report is intentionally temperate and condones a good deal of commercial practice because it is almost impossible to do otherwise.

We take the following from the Report:—

'The responsibility of relaxing the principle of retaining inviolate the purity of the flour supply is a very grave one: *flour should contain no added substance*. Whilst it has been urged that the use of Acid Calcium Phosphate, sulphates, and persulphates, merely contributes to the phosphates and sulphates normally present—a not entirely tenable assumption—it is obvious that Nitrogen and Benzoyl Peroxide, Chlorine and Nitrogen Trichloride, are foreign to flour. *Chlorine* probably inhibits the nutritive value of gluten by entering into the *Tyrosin and Tryptophane* groupings, possibly forming *products which may act injuriously*. Although feeding experiments with rats (using flour bleached with chlorine) gave inconclusive results, yet the Committee for chemical reasons *considered its use* and that of *Nitrogen Trichloride as undesirable*. The use of small amounts of Nitrogen Peroxide, Benzoyl Peroxide, Persulphates, Acid Calcium and Acid Ammonium Phosphates, was not condemned, but the Committee considered that physical methods of improving flour should be investigated, so that *chemical improvers may be entirely superseded*.'—Rept. Dept. Com. on Treatment of Flour with Chemical Substances, 1927.

This Report is gratifying.

Oleum Morrhuæ.—It has been found that the Vitamin content is in the order:—Scotch, Newfoundland, Norwegian.

Opium.—It is stated that a poppy grown in this country does not elaborate Morphine. The point that interests us is whether we can *make Papaver Somniferum* do so profitably by intensive cultivation; we hope to experiment in that direction.

Phenoltetrabromphthalein Sodium Sulphonate has been successful as a liver function test. A further test that has attracted attention is the Rose Bengal Elimination Test. This Fluorescein derivative passes almost entirely from the blood stream through the liver. It remains in the circulation long enough for determination in the plasma.

The Diazo Reaction in the urine, which was discarded some years ago in respect of typhoid, has been employed under the designation Van den Bergh Reaction for obstructive or impaired liver function.

Plumbum.—The possibility of a painter absorbing Lead is now greatly reduced by the requirements of the Lead Paint (Protection against Poisoning) Act, *v. p.* 149. We deal with the effects of Lead absorption on *p.* 150, both in respect of paints and enamels and of the recently popularised Tetra-Ethyl Lead. With regard to the latter, the labelling of Petrol cans and pumps, and other warnings are provided, as advised in the Interim Report of the Departmental Committee of the Ministry of Health. Drivers and garage employees have given no definite signs of poisoning after exposure for two years, but there is difficulty in recognising the poisoning effects. Many protest against the use of 'Ethyl' Petrol.

Quinine.—We have for some time past advocated the use of the alkaloidal base in a suitable medium when required for injection, e.g., in the form of Mannitol-Quinine, as the salts are frequently badly tolerated, even to the extent of producing necrosis. We showed that this and other alkaloids when injected as ordinary salts, e.g., the Sulphates or Hydrochlorides, actually function in the form of alkaloidal bases.

We notice an investigation shows that 75% of Quinine added to blood can be recovered. It is carried by adsorption.

Strophanthus has been the subject of biological assay against a Standardised Ouabain solution. The Official *S. Komôé* is still mixed with adulterants though the 'pure' drug can be obtained unmixed by paying for it.

Thallium Acetate. In our opinion the less said about this method of epilation the better. We give information additional to that in Vol. I.

ANIMAL ORGANO-THERAPY.

Pituitary.—The League of Nations Commission on Standardisation of Serums, Serological Reactions and Biological Products has definitely adopted an International Standard for the evaluation of Posterior Lobe Pituitary preparations. With regard to clinical use it is advised that small doses of 2 units should be available for hastening labour at certain stages.

The oxytocic and pressor principles are now separated and are available commercially.

Thyroid.—A modified Hunter's Method is described, but the Nitrite and Petroleum-Ether method, which has been in *The Extra Pharmacopœia* for seventeen years, would, we believe, prove more accurate. The Sodium Thiosulphate titration might be obviated by colorimetric assay against Standards (*cf.* our remarks on methods of assay of Iodine in Natural Waters).

As to Iodine content, we found (June 1929) 0.378% in material from the Argentine, which is certainly satisfactory in comparison with findings in earlier years.

Thyroxin.—The *locus standi* of this previously termed active principle does not appear even now to be entirely elucidated. It may, according to a recent 'Leader,' be an intermediate (*v.p.* 174).

Concerning Gland preparations in general, certain ratios between desiccated and fresh material have been agreed upon (*v.p.* 175).

RECOGNITION OF ORGANIC CHEMICALS.—With regard to the Charts (*p.* 206 *et seq.*) we tried to determine the most suitable recognition tests that would show small amounts of the compounds in question, and in addition to state the *minimum* quantities that can be found under definite conditions. Text-books are in the habit of stating, *e.g.*, such-and-such test will show 1 per 10,000, or of using similar phraseology, but this does not always help the analyst.

The research we have in mind is laborious, involving considerable expenditure of time and a great number of experiments.

We have shown our findings re *Minimum Detectable Quantities* in the following instances, *inter alia* :—

Acetanilide, Acetone, Acetophenone, Acid. Aceto-Salicylic, Acid. Benzoic, Acid. Cinnamic, Acid. Gallic, Acid. Glycerophosphoric, Acid. Hippuric, Acid. Salicylic, Aconitine, Aloin, Antimony Potassium Tartrate, Arrhenal, Arsamin, Caffeine, Chloral Hydrate, Cinchonidine, Cocaine, Digitoxin, Emetine, Ethyl-Morphine Hydrochloride, Luminal, Saccharin, and Sparteine Sulphate.

New to the Chart are: Aspriodine, Hexyl-Resorcinol, Magisal, Mercurochrome, Methyl-Aspriodine, Phenyl-Aspriodine, Phenyl-Sedasprin, Sedasprin, Tetrabromphenolphthalein, Tetraiodophenolphthalein, Trional, Tylcalsin and Tyllithin.

ANTISEPTIC POWERS of CHEMICALS.—A Public Health authority has shown that the Poisons and Pharmacy Act of 1908 fosters (quite unintentionally) the sale at oil and grocery stores, of comparatively ineffectual disinfecting fluids containing less than 3% of Phenol, or its homologues.

To conduct the generally recognised Rideal-Walker method of testing is somewhat of a time-consuming proposition. Modifications continue to be introduced, *e.g.*, using *Staphylococcus aureus*. This step would certainly appear to raise the standard of antiseptics and to 'weed out' the weak ones, because of all non-sporing bacteria *Staphylococci* are the most resistant to desiccation, heating, and germicides. Even 100° C., if of only a few minutes' application, may fail to sterilise.

We have no special experience in employing this test organism. Our data on nearly 200 antiseptics, which we have accumulated since 1908, are mainly centred on stating whether the disinfectant in question will kill *B. coli* in a reasonable time, such as $2\frac{1}{2}$ minutes. This forms, we think, a useful criterion to work with.

Catgut ribbons, it is said, immersed in 1 in 1,000 Mercuric Iodide (presumably with Potassium Iodide) for 1,710 days were infected at the end of that time. This is remarkable and needs further investigation.

The Flavine antiseptics are much used as vesical injections and in gynæcology, being efficacious in the presence of serum, but their antiseptic power as ordinarily determined is rather slight. This brings to mind a problem which was submitted to us in respect of an antiseptic of known caustic effect, namely, Phenol. It was suggested that Carbolic Glycerin, as an injection in labour, might be of value in preventing puerperal infection. The exact proportion of the antiseptic in the Glycerin is however open to discussion. The problem is in effect divisible under several headings:— (1) The strength must not be sufficient to injure the membranes or to cause shock. (2) It is known that Glycerin may weaken the antiseptic potency of Phenol. (3) On the other hand, Glycerin in itself is antiseptic, and (4) its physical qualities are ideal for the purpose under consideration.

We confirmed (1929) that the bacterial efficiency of Phenol in Glycerin is actually less than in an aqueous solution. One is guided in endeavouring to decide a suitable strength, by that of the various (aqueous) injections used in hospital practice, and the conclusion appears to be that 1% would be effective, and that stronger solutions would introduce a considerable element of risk. The subject is set out on *p.* 273. We do not recall having seen the matter discussed in medical literature.

As a further suggestion, one would think Thymol in Glycerin worth trying—here also similar difficulties arise, and it might possibly be vetoed on account of its excessive smarting effect, though this is transient.

IONTOPHORESIS.—The writer recently estimated the Potassium Iodide in a solution which had been applied on a pad to a patient suffering from arthritis, a high ampèreage being employed (100 to 200 m.a.), and compared it with the content at the commencement. The amount ionised which had been 'driven in' was much in agreement with that of statements by previous workers, who had proceeded on somewhat different lines, namely, by estimating the iodine in the excreta (*v.p.* 287).

RADIOLOGY.—It is thirty-four years since Röntgen Rays were discovered, and the boon of their discovery becomes more evident every day.

We deal with the subject in the following divisions:—

Apparatus, Diagnosis, Reviews of Treatment, Dosage, Dangerous Effects, Protective Materials, High Frequency Current, Diathermy, Flinsen Light, Ultra-Violet Light, Heliotherapy, etc.

In the matter of treatment, as a surgeon wrote recently, three periods can be traced: (1) the period of inadequate and tentative dosage: (2) the ushering in of the Coolidge Tube and the intensive Erlangen technique: (3) the period dating from the recognition of the failure of the Erlangen methods, and the use of the modern tube in divided doses (*v.p.* 300).

We place the diseases and affections treated in an approximately alphabetical position (*v.pp.* 301–306), ranging from acne to whooping cough.

Under Malignant Disease—Cancer of the Breast—the statement occurs that as far back as 1926 intensive penetrative rays were found positively harmful, and it is further pointed out specifically in the chapter on the Erlangen Treatment that the results recorded in the past have not been obtained by others.

Dosage.—The X-Ray Unit Committee at the **Second International Congress of Radiology**, held at Stockholm in August 1928, adopted an International Unit, to be termed the Röntgen ('R'). This agreement enables radiologists in different countries to reproduce accurately an X-ray dose needed, and comparisons of results are therefore more possible than hitherto (*v.p.* 306).

Recommendations as to methods for relieving X-Ray burns are given.

A death by electrocution through the medium of a wireless head-phone, in consequence of faults in an electric lamp standard circuit and a further bare wire in the telephone circuit, is referred to.

The Finsen Arc Lamp has been improved in the direction of reducing the heat of the light column, thus minimising pain and giving an increase of irradiation intensity.

Ultra-Violet Light.—A somewhat exhaustive account of the penetrative powers of various Angström units—their action on the tissues, effect on the skin and body, apparatus, method of exposure, and diseases and patients in which the treatment is likely to be harmful, has been provided by a specialist in this branch of science, and the treatise is available *in precis* on *p.* 316.

A recent Medical Research Council Report has made certain monetary comparisons between Ultra-Violet Rays and Cod Liver Oil, in respect of the supply to the body of Vitamin 'D,' and the comparison certainly reflects adversely on the Ultra-Violet Light.

The danger of Ultra-Violet Light when operated by unskilled persons is dwelt upon. At the 1928 B.M.A. Meeting it was agreed that a Register of qualified Electrotherapeutists should be compiled, while the Presidential Address of the 1929 Meeting made it clear that the rays are far from innocuous: chronic nephritis, arteriosclerosis, and quiescent tuberculosis, are adversely affected. The Society of Apothecaries of London, with the British Medical Association have undertaken to set up a standard of proficiency, and to keep a Register of 'Biophysical Assistants' ('B.P.A.').

There are some very interesting comments on the source of Ultra-Violet Light, and its conservation in our cities. We were struck

by a practical suggestion which has been put forward to use windows of Cellophane, between wire gauze.

Ultra-Violet Light therapy is advocated in rickets, in surgical tuberculosis, in some neurological conditions, in anæmias and skin affections. We deal alphabetically with the diseases which have been under treatment, from alopecia to rheumatic affections (see pp. 319-320), and, under General Notes on Treatment its limitations are further dealt with.

Sugar Synthesis.—An English discovery, to which we think too little attention has been paid, is the synthesis of sugars by the action of Ultra-Violet Light on solutions of Carbon Dioxide, in which Nickel Carbonate is suspended.

A slight confusion, in our opinion, has been occasioned by applying the name **Heliotherapy** to Ultra-Violet Light and similar types of medical irradiation. The name should surely be conserved for the employment of natural sunlight.

Even natural sunshine may prove harmful in cases of excessive exposure.

RADIUM.—We remark on the extremely unsatisfactory position of the commerce of Radium. The existing monopoly is scandalous and from all aspects is to be regretted. We recently had to wait months for delivery of a few milligrammes needed by a practitioner in a South American State. After suffering a long delay, he wrote saying he thought that certain International friendships indicated that our mediation might be more effectual in expediting delivery than a communication direct from him to the concern which now holds the whip-hand—the word is not ill-chosen.

Random empiricism in Radium Therapy is giving place to more scientific methods; early cancer of the neck of the womb can now be removed by Radium as certainly as by the knife, and for cancer in other parts of the body Radium will soon replace excision. There are further eulogies, e.g., in five years it is claimed, the knife will be of secondary importance in malignant disease.

A comparison has been made between Radium treatment in this country and in France and Belgium, especially with regard to the use of **Radon**. The French methods are said to be in advance of ours.

Twenty years ago when tube-form applicators of Gold, Silver, Platinum and Aluminium, usually of 2 mm. in thickness, were filled with unimpeachable Radium Bromide (costing eight shillings a milligramme) for the late Sir J. Mackenzie Davidson and other specialists, the Radium was loose in the container. The only change in design of tubes and needles since that day is that the Radium is now compressed into the container, which has a uniform thickness of the wall (0.5 to 1 mm.). Platinum is chiefly used, and the nomenclature has been revised a little—the name applicator being applied to devices for holding the containers in position. '*Linear intensity*' is a factor of importance.

Screened Radon Seeds for implanting have the obvious advantage of economy, so far as the parent element is concerned. The initial response with this is said to be more rapid than with other forms of Radium Therapy.

'**Bomb**' Treatment is likely to prove the method of choice in Radium Therapy, but the high cost and restricted supply of Radium require urgent attention. Economy is necessary—the work should be specialised in special institutions, and 'night' and 'day' staffs employed.—Presidential Address, B.M.A. Ann. Meeting, 1929, per B.M.J. ii./29, 134.

The Chapters on the **Analysis of Urine, Blood, Fæces, Cerebro-spinal Fluid etc.**, have been drastically revised and the various sections almost entirely re-written. It was felt that these pages were too replete with abstruse opinions on unsettled points in methods of diagnosis.

Nevertheless, we have adopted a catholic spirit and a policy *tenere mediam viam*. For example, certain Albumin Tests may be only occasionally used, yet the pharmacist must have these available for reference, as in cases of doubt it is of the utmost importance to be able to state that *e.g.* two or three specified tests gave conclusive evidence.

The general effect, we trust, is to give the medical man a series of quick and reliable methods such as are employed in London hospitals devoted to the treatment of genito-urinary diseases.

It is curious that certain tests gain popularity, due no doubt to a better 'press,' while others go virtually unnoticed. A case in point occurs to us with regard to **Fehling's Test, Gerrard's Modification of Fehling, and Benedict's Tests**. The end point with the second is more definite than with the others and it should be more often employed—we have occasion to use it in our laboratory almost daily.

Renal Function Tests are described with concise instructions. The diagnosis may be either by (1) Systematic examination of the urine, (2) Blood Test, or (3) Elimination Test. Of the last, the Indigo-Carmine and Phenol Red methods seem to be the most satisfactory. The Diastase Test appears to be of poor utility.

Water Analysis.—We have already referred in this Preface to the matter of Iodine in natural waters, which has interested us. *Vide Iodine.*

A new formula for **Nessler's Reagent** is provided. We have found it far more delicate than the one in the *British Pharmacopœia* 1914.

We provide a review of the **ANNUAL WATER BOARD REPORTS** up to and including the 22nd Report for 1927. Attention is drawn to the reiterated utility of **Chlorination**. It almost completely removes *B. coli* and was recently effective against *leptospira*. The Molesey supply in respect of *B. coli* was found to be 1,000 times better than the raw river water, the former containing *B. coli* in 100

Cc. in 39% of samples and the latter *B. coli* in 0.1 Cc. in 50% of samples. It would thus be less risky to drink 50 pints of stored water than 1 ounce of the native Thames.

MILK.—We have been much engrossed on what we would call the Milk Problem. We have considered cow's milk from the aspect of the Legislature, the Medical Officer of Health, the Veterinary Surgeon, the Dairy Farmer, the Analyst, and, most important of all, the consumer. We have discussed the matter personally with an Official at the Ministry of Agriculture and Fisheries: we have interviewed the Staff of the Royal Veterinary College: we have sought the dairy farmer's view, and we have conducted research on the data obtained.

In referring the reader to *pp.* 464 to 485, we would summarise here the range of our studies, saying at once that the more we investigated the matter the less satisfied we became, and our advice to any individual who has the opportunity, would be to keep a few cows himself, rear his own stock, and exercise his own control over it.

We give a résumé of all the Enactments that have resulted from Parliamentary efforts since 1915, in which year the **Milk and Dairies (Consolidation) Act** was passed, although it did not come into force until 1925.

The Act leads off by placing the onus (rightly) on the local M.O.H. to stop the sale of tuberculous milk, and Section 10 enacts that Veterinary Inspectors of cattle may be appointed by the local authority.

The **Milk and Dairies Order of 1926** followed; this required local councils to inspect cattle by means of Veterinary Inspectors *after* (!) tuberculous milk has been found.

An Amendment Act was passed in 1922 and in 1923 the **Special Designations Order** came into operation—a palliative measure which has been dubbed a “magnificent educational gesture.” To our mind, this latest Order evades the main desiderata (1) of eradicating tuberculosis from herds, and (2) of controlling *all* milk in respect of *B. tuberculosis*. Few members of the public, we consider, could be expected to differentiate between the types of milk offered under this Act.

Certain Orders of a similar type are applicable to Scotland.

We provide the main features relative to Graded Milks and the methods of testing cattle with Tuberculin, namely, the Intradermal and Ophthalmic Reactions. Recently a Modified Intradermal Test was introduced, involving two injections. The Ophthalmic Test has been thought unreliable.

The **Tuberculosis Order of 1925** places the responsibility for owning a tuberculous cow upon the owner, and a Veterinary Inspector may enter premises in which a cow is kept at any time

and examine the animal, which on a positive finding must be slaughtered.

Veterinary opinion (*v.p.* 478) is very outspoken on the matter of inspection and control. We entirely agree that it is the Veterinary Surgeon's job to detect tuberculosis in cattle and we give the views of several Professors of Veterinary Medicine and of a Veterinary Surgeon in practice. One of the former stated '*No milk is used in my house without being boiled,*' and the latter: '*All cases, whether open or not, are a potential source of danger and should be so treated.*'

We are indebted to the Chief Veterinary Officer of the County Council of the West Riding of Yorkshire for the following:—

"Dairy inspection of cows in Scotland is obligatory at least once a year, but in England the Milk and Dairies Order gives power to carry out such inspections as are thought necessary by the local authority concerned, there is however no obligation. The result is that each local authority does what it likes, and whether whole or part-time inspections, or none at all, are conducted, depends upon a variety of circumstances.

As far as I know, the following Counties in England have now regular veterinary inspection of cows by whole-time officers:

Cumberland (first to begin)	Surrey
Yorkshire (West Riding)	Durham (about to commence)
„ (North Riding)	

A certain amount of regular inspection is done in Herefordshire. Gloucestershire operates by part-time veterinary service. As time goes on, more Counties will no doubt gradually follow suit, *when the public begins to realise the necessity.*"

To gauge to an extent the magnitude of the undertaking, we notice in the Second Annual Report of the West Riding Council the statement that the whole-time Veterinary Staff covered 75,612 miles in one year in the execution of their duties.

It is stated in this Report that the Tuberculosis Order of 1925 has proved of great benefit in ensuring destruction of affected cows. 809 cows were slaughtered in 1928-29, as compared with 898 for the previous year, the total numbers examined being respectively 16,870 and 21,078. Of the cattle slaughtered 68.6% were 'advanced' cases and 30.8% 'non-advanced' (as compared with 75.4% and 24.05% for the previous year). 28.2% were suffering from udder tuberculosis, as against 16.2% the previous year, the increase being largely due to detection by routine inspection, few cases being reported by the owners. ***Many of these cows had already been milking for some time and it is impossible to say what damage they may have done.*** Tuberculous cattle not reported are often sent direct to the knacker or otherwise disposed of by the farmer."

Before leaving the matter, we would draw attention to the findings of The Royal Commission on Human and Bovine Tuberculosis, 1907-1911, to the effect that "A considerable proportion of the tuberculosis affecting children, particularly of the abdominal organs and cervical glands, is of bovine origin. Infection by cow's milk, and beef and pork is possible. Infants and young children are specially susceptible to infection by the bovine bacillus, but even in adolescents and adults the same sources of infection are possible dangers, though to a less extent." The Government was urged to take action to prevent consumption of infected milk and meat.—*B.M.J.* ii./11,122, *L. ii.*/11,166.

We follow with a dissertation on Pasteurised Milk—the first paper dealing with the 1923 Ministry of Health Report, a Report

highly favourable to this method as a safeguard of the public health.

In the process of Pasteurisation a small proportion of the tubercle bacilli may escape actual destruction. It is said that the virulence of those bacilli is so impaired as to make them harmless, but we fear this is not the fact, and both medical and veterinary authority could be produced to prove our contention. There is no doubt, however, that Pasteurisation reduces the general bacterial count. This is shown by figures which we give, taken under actual working conditions.

It is very clear from the efforts of Associations interested in clean milk without the intervention of Pasteurisation that the purveyors of the Pasteurised article are not holding the field undisputed. Actually the proportion of Pasteurised Milk supplied in 1927 was from 5 to 10% of the total.

Work has quite recently been carried out on the matter of the **Diffusible Lime Content**.—(v.p. 475.)

We have found a loss both in regard to Diffusible Calcium and in Phosphate caused by Pasteurisation.

We conclude our survey of the Milk Problem with a suggestion (p. 483) relative to a 'direct' supply of milk in **Thermo-isolated vessels**. We cannot help thinking there are advantages in such a scheme—we view it as an idea of the future.

The quality of **Margarine** is now protected by the **1928 Food and Drugs (Adulteration) Act** (v.p. 491), which repeals and re-enacts the provisions of Acts dating from 1875 about Food and Drugs (with the exception of a few Sections relative to dealings in Tea).

Food Preservatives.—We give the entire list of permitted preservatives for various foods, together with the permissible quantities in parts per million. No other preservatives are allowed.

Mould Inhibition by means of various Preservatives.—An investigation was carried out with five common moulds and numerous preservatives. Sulphurous Acid was found to be the most effective. The problem is interesting, because there are many pharmaceutical preparations which are prone to mould growth and hence cause considerable annoyance.

Bacteriological Notes.—In this section we bring together some information on what may be called 'special' diseases, dealing particularly with their bacteriology and epidemiology. Revision has been necessary under many headings, e.g., *Acne*, *Blackwater Fever*, *Botulism*, *Cancer*, *Diphtheria*, *Dysentery*, *Epidemic Encephalitis*, *Leishmaniasis*, *Leprosy*, *Malaria*, *Measles*, *Plague*, *Poliomyelitis*, *Scarlatina*, *Syphilis*, *Tuberculosis*, *Trypanosomiasis*, *Yaws*, *Yellow Fever*, etc.

With regard to **Cancer**, the matter available is voluminous. It is subdivided into Reports of Cancer Research Organisations,

Recent General Papers, Diagnosis, Theories, Filter-passing Virus, Irritants, Death-rate and Statistics, and Treatment.

A Report of the **International Conference on Cancer**, held in July, 1928, is given on *pp.* 513-517. There follow, *inter alia*, Ministry of Health Reports, and Reports of the Manchester Campaign and of the League of Nations Enquiry.

It is regrettable that after so large a volume of knowledge, in reality mainly research on the *cause* of cancer, only a page or so can be devoted to *Treatment*, and that mainly in respect of Lead (*v.* also Vol. I., *p.* 1042). The use of Fluorescein painted externally and given internally is also described.

Diphtheria.—The method of carrying out the Schick Test is given. It has been tried on 50,000 school children in this country, followed by immunisation in positive cases, and practically none of these has since contracted diphtheria. It is hoped the use of Toxoid instead of Toxin-antitoxin mixture will prevent recurrence of fatalities which have occurred on one or two occasions. On the other hand, a criticism from the U.S.A. is to the effect that the test is of academic interest only.

Dysentery.—The differences between *Entomæba histolytica* and *E. coli* are tabulated for reference.

Encephalitis.—The relationship between acute poliomyelitis, cerebro-spinal fever, and encephalitis lethargica is dwelt upon, and reference is made to post-vaccinal encephalitis.

Leishmaniasis.—The subject matter is re-written to meet the latest views re Kala-azar, Oriental Sore, and Espundia (*etc.*), with their various synonyms.

Leprosy.—New facts as to its etiology are dealt with at some length.

Measles.—Seroprophylaxis, employing serum to achieve passive immunity.

Plague.—HAFFKINE'S VACCINE has saved several million lives.

Poliomyelitis.—Convalescent serum intramuscularly has been found of distinct value.

Scarlet Fever.—The *Schultz-Charlton Blanching Test* and the *Dick Test* call for mention.

Small Pox and Vaccination are dealt with in Vol. I., but the following recent Order may be noted :

The VACCINATION ORDER, 1929 (framed on the Report of the Rolleston Committee) instructs Public Vaccinators to make single insertions of lymph instead of the previous 4 insertions, multiple insertions being available to those desiring them. Re-vaccination is to be encouraged at the ages of 5 to 7 and 14 to 16. In a covering letter, the importance of primary vaccination in infancy is emphasised, and as 'post-vaccinal nervous disease' occurs mainly in children of school age or adolescents who have never been vaccinated, it is not considered wise to press for vaccination of such

persons (unless directly exposed to infection) while the small-pox prevalent in this country retains its mild character. The new Order came into force on Oct. 1, 1929. (L. ii./29,399,411.)

Reference has already been made to post-vaccinal encephalitis.

Syphilis.—The Sachs-Georgi and the Kahn Test are described.

Trypanosomiasis.—On *pp.* 589–591 are the results of the International Conference together with the final Report of the League of Nations Commission. A number of references to the literatures are given. Tryparsamide is the most efficient drug so far available.

Yellow Fever is probably caused by a filter-passing virus.

The author is indebted to several medical men for their advice in preparation of the issue and in particular is grateful to W. K. Fitch and A. J. V. Field, Pharmacists; F. G. Dewdney, chemist; and Sydney Ward, as secretary, for help in many matters connected with the volume.

Investigations have been begun in collaboration with the Medical Research Council on a systematic survey of various organic chemical nuclei and substituent groups more particularly with reference to the preparation of therapeutic agents for the treatment of sleeping sickness, kala azar, malaria and other endemic diseases. The writer had the opportunity recently of visiting at Teddington the Chemical Research Laboratory of the Department of Scientific and Industrial Research where a group of workers was engaged under the direction of Professor G. T. Morgan, F.R.S., in the study of organic antimonials, compounds allied to the Bayer 205 Series and other organic substances.

The products of these researches are being submitted to the Chemotherapy Committee of the Medical Research Council in the hope that further experimental evidence may be gained on the relationships between chemical constitution and physiological activity thus leading to drugs of greater potency and easier applicability than those at present employed as remedial agents.

The workers in such a field will, we fear, meet many disappointments, since hundreds of substances will probably be examined before one of outstanding merit is discovered, but nevertheless, these problems are matters of vital concern. We hope that the labours of these scientists may prove fruitful for the Empire and for suffering humanity in general, and that they may be welcomed by scientists abroad in an International spirit of welfare.

W. HARRISON MARTINDALE,
October, 1929.

INTRODUCTION.

The information regarding *Materia Medica*, Supplement and Animal Organotherapy, pp. 1 to 175, dealt with in this volume, is arranged in the same sequence as in the corresponding [sections of Vol. I.

The question of POISONS (in the light of the Poisons and Pharmacy Acts and the Dangerous Drugs Acts), has not received full consideration in this volume, as circumstances hardly necessitate it. In Vol. I., however, we indicate into which part of the Poisons Schedule any substance falls, by means of the signs **P1** and **P**, and in addition we show whether a “drug” or a preparation comes within the requirements of the Dangerous Drugs Acts by the letter **D**.

Vol. II.—CROSS REFERENCES in the following pages are in heavy type, thus, **100**.

CORRIGENDA TO VOL. I. (19TH EDN.)

p. 731, line 32.—Under *Soluté de Quinine pour Injection hypodermique Fr. Cx.* For Quinine Acid Hydrochloride read *Quinine Hydrochloride*.
p. 740.—Quinine Urethane is **P**.

NOTES.

Suggestions from readers will be appreciated.

ABBREVIATIONS.

When the reference is to a periodical, the number put first is the number of the volume; then follow the last two figures of the year, and the last number refers to the page, thus, B.M.J. ii./29,500.

- A.R.—List of Reagents for Analytical Purposes prepared by a Special Committee appointed by the Councils of the Institute of Chemistry of Great Britain and Ireland and the Society of Public Analysts and other Analytical Chemists.—London, 1915.
- Allen.—Allen's Commercial Organic Analysis.—Edited by H. Leffmann, M.A., M.D., W. A. Davis, B.Sc., A.C.G.I., and S. S. Sadtler, S.B.. Fourth Edn., 1909-1917, 9 vols.; also Fifth Edn. of Vols. I. to IV. (1924-5); Vol. V. (1927); Vol. VI. (1928); Vol. VII. (1929).
- Am JI.Ph.—American Journal of Pharmacy.
- Anal.—Analyst, W. Heffer and Sons, Ltd., 4, Petty Cury, Cambridge.
- Arch. Radiol.—Archives of Radiology and Electrotherapy of the British Assoc. for Advancement of Radiol. and Physiother. See also 'J.R.S.'
- B.C.A.—British Chemical Abstracts. Branch A—pure Chemistry—is issued monthly with the Journal of the Chemical Society, London.
- B. & C.P.—British and Colonial Pharmacist, London, previously B. & C.D.
- B.J.R.—The British Journal of Radiology, W. Heinemann, London. See J.R.S.
- B.M.J.—British Medical Journal, London.
- B.M.J.E.—British Medical Journal Epitome.
- B.P. '14.—British Pharmacopœia 1914 (previously indicated, *Off.*).
- B.Pt.—Boiling Point.
- B.P.C.—British Pharmaceutical Codex, 1923.
- B.P.C. 1894 or 1901—Formulary of the British Pharm. Conference.
- Barnett.—Preparation of Organic Compounds—E. De Barry Barnett (Churchill), 1920.
- Batty Shaw—Organotherapy, or Treatment by means of preparations of Various Organs, H. Batty Shaw, M.D., F.R.C.P.
- Bayliss.—'The Colloidal State and its Medical and Physiological Aspects.'—by the late Sir W. M. Bayliss, 1923.
- Beddoes.—Syphilis, Its Diagnosis, Prognosis, Prevention and Treatment, T. P. Beddoes, 1909.
- Berl. Klin. Woch.—Berliner Klinische Wochenschrift, Berlin.
- Bosanquet.—Serums, Vaccines and Toxins in treatment and diagnosis, W. Cecil Bosanquet, M.D., 3rd Edition, 1916.
- Brompton H.—Pharmacopœia of the Hospital for Consumption and Diseases, of the Chest.—Brompton, Eleventh Edn., 1928.
- Brooke.—Tropical Medicine, Hygiene and Parasitology, by Gilbert E. Brooke, 1920.
- C.D.—Chemist and Druggist, London.
- C.H.W.—Formulæ of Chelsea Hospital for Women, 1900.
- C.L.T.E.—Central London Throat and Ear Hosp. Pharm., 1924 and earlier.
- C.R.—Changes proposed in the British Pharmacopœia by the International Agreement for the Unification of Pharmacopœial Formulas for Potent Drugs, Brussels, Nov. 29, 1906, from a report to the Pharmacopœia Committee of the General Medical Council. Adopted March 4, 1907. This Committee issued further reports in 1908, 1910, 1911. cf. F.I.
- C.X.—Charing Cross Hospital Pharm., 1922.

- Can. Form.—The Canadian Formulary of Unofficial Preparations.
- Chemical Abstracts.—Published by the American Chemical Society.
- Chininum.—Chininum Scriptones Collectæ, Bureau for increasing the use of Quinine, Amsterdam, 1925.
- Clin. Jl.—Clinical Journal, London.
- Colyer's Dental Surgery and Pathology.—Fifth Edn., 1923 and earlier issues (previously Smale and Colyer's Diseases and Injuries of Teeth).
- Comptes Rend.—Comptes Rendus Hebdomadaires des Séances de D'Académie des Sciences.
- Cushny.—Text Book of Pharmacology and Therapeutics, by the late Arthur R. Cushny, M.A., M.D., F.R.S., 8th Edition, 1924.
- D.M.W.—Deutsche Medizinische Wochenschrift. Leipzig.
- ☐.—Drugs or preparations coming within the scope of the Dangerous Drugs Acts, 1920 and 1923, and Consolidated Regulations, 1928.
- Dawson Turner.—Radium, its Physics and Therapeutics, by Dawson Turner, B.A., M.D., 2nd Edition, 1913.
- Digitalis Assay.—W. H. Martindale. A communication to the Pharmaceutical Society of Great Britain, 1913. (H. K. Lewis & Co., Ltd.)
- Disp.—Art of Dispensing, published by *The Chemist and Druggist*, London, 10th Edition, 1926.
- Dixon.—Manual of Pharmacology, 6th Edn., 1925, W. E. Dixon, M.A., M.D., F.R.S.
- E.—Pharm. of Evelina Hospital, Southwark, 1906.
- E.G.A.—Elizabeth Garrett-Anderson. Hosp. Pharmacopœia, 1926 and earlier Edns., Euston Road, London (formerly New Hospital for Women).
- E.L.—Pharm. of East London Hospital for Children, 1915.
- Ec.Prod.I.—Economic Products of India, 1889–96.
- Ed.M.J.—Edinburgh Medical Journal.
- Edition XVIII.—Eighteenth Edition of this work (1924). For References and comments unavoidably deleted.
- Emery.—Clinical Bacteriology and Hæmatology, W. D'Este Emery, M.D., B.Sc., 6th Edition, 1921.
- Evans.—Evans' Analytical Notes.—Evans Sons, Lescher and Webb, Ltd., London and Liverpool.
- F.E.—Farmacopea Española Septima Edicion, 1905. Madrid.
- F.I.—Formula Internationalis, International Agreement for Unification of Formulas signed 1906—*cf.* C.R. *antea*. Also Agreements made at Second International Conference at Brussels 1925 as stated in Final Report and Preliminary Draft. (P.J., ii./25,547; i./26,56), see also P.J. i./26,41,42,294; ii./26,734; ii./27,372.
- F.N.—Formulaire des Médicaments Nouveaux. Bocquillon-Limousin.
- F. Norsk.—Den Norske Farmakopæ, 1913. Norwegian Pharmacopœia.
- Fr. Cx.—Codex Medicamentarius Gallicus, Pharmacopée Française. Paris, 1908, Matson et-Cie, 120, Boulevard Saint Germain.
- Fr. Cx. Supp. I. to V.—Supplement I (1920) to V, (Official from Apl. 5,26); also 'Nouveau Supplement,' 1926, issued in book form.
- Finnemore.—Essential Oils, their Chemistry and Technology.—H. Finnemore, 1926.
- G.—The Essentials of Materia Medica and Therapeutics—Sir A. E. Garrod, M.D., and Sir N. J. C. Tirard, M.D., 13th Edition, 1890.
- G.H.—Pharmacopœia of Guy's Hospital, 1916.
- G.N.C.—Pharm. Gt. Northern Central Hospital, 1908. (See also R.N.H.)
- Garrod.—Sir A. E. Garrod, D.M., M.A., Inborn Errors of Metabolism, 1923, and other communications.
- Gehe.—Gehe's Codex der Bezeichnungen von Arzneimitteln, 5th Edn. 1929 (Dresden) and earlier issues.
- Ghosh.—Treatise on Materia Medica and Therapeutics, by the late R. Ghosh, L.M.S., Cal. Univ. Edited by B. H. Deare, Lieut.-Col. I.M.S. 11th Edition, 1927 (and Abstracts from earlier Editions).
- Glyn-Jones.—The Law of Poisons and Pharmacy. Sir W. S. Glyn-Jones.
- Gould.—Gould's Medical Dictionary, by G. M. Gould, A.M., M.D., 8th Edition, 1926, and earlier issues.
- Gradwohl and Blaiwas.—"The Newer Methods of Blood and Urine Chemistry," by R. B. H. Gradwohl, M.D., Director of the Gradwohl Laboratories, Chicago and St. Louis, and A. J. Blaiwas, St. Luke's Hospital (Chemical Laboratory), New York. Sec. Ed., 1920.

- Gt. Orm. H.—Gt. Ormond St. Hosp. Children Pharm., 1927.
- Green.—Green's Encyclopedia of Medicine and Surgery.
- H.—Text Book of Practical Therapeutics, Hobart Amory Hare. 19th Edition, 1925 (and abstracts from earlier Editions).
- H.W.—W. Hale White, M.D., *Materia Medica, Pharmacy, Pharmacology, and Therapeutics*, 19th Edn., 1927, and previous issues.
- Hager.—Handbuch der Pharmaceutischen Praxis, 1907 and 1925.
- Hewlett.—Serum and Vaccine Therapy, T. R. Hewlett, 2nd Edition, 1910, also Bacteriology, 8th Edition, 1926.
- Hutchison.—R. Hutchison, M.D., F.R.C.P., *Food and Principles of Dietetics*, Edward Arnold, London, 4th Edition, 1916.
- I.C. Add.—Indian and Colonial Addendum (1900) to the B.P., 1898.
- I.D.C.—Indigenous Drugs Committee, 2nd Report, Simla; 1909. Third Report, Calcutta, 1916.
- I.M.G.—Indian Medical Gazette.
- I.V.—Iodine Value.
- Int. Conf. Trop. Am.—Proceedings of the International Conference on Health Problems in Trop. America, 1924, United Fruit Co., Boston.
- Int. Cong.—VIIth International Congress of Applied Chemistry, London, May, 1909 (papers read at); also VIIIth Congress, Washington, 1912.
- J.C.S.A.—Jl. of the Chem. Soc. Abstracts. London. See also B.C.A.
- J.C.S.T.—Journal of the Chemical Society. Transactions. London.
- J.R.S.—Journal of the Roentgen Society, London, and as from Jan. 1924 "The British Jl. of Radiology, Rontgen Society Section, incorporating the Jl. of the Rontgen Society." See also Arch. Radiol.
- Jl. A.M.A.—Journal American Medical Association, Chicago.
- Jl. Am. Ph.A.—Journal of the American Pharmaceutical Association.
- Jl. Ph. and Exp. Ther.—The Journal of Pharmacology and Experimental Therapeutics. Edited by J. J. Abel (The Johns Hopkins University, and Walter E. Dixon (University of Cambridge). Baltimore and London)
- Jl. R.A.M.C.—Journal of the Royal Army Medical Corps (Mthly.).
- Jl. R.N.M.S.—Journal of the Royal Naval Medical Service (Qtrly.).
- Jl. Trop. Med.—Journal of Tropical Medicine and Hygiene, London.
- K.C.H.—King's College Hospital Pharmacopœia, 1927.
- Knox.—Radiography, X-Ray Therapeutics and Radium Therapy, by Robert Knox. 3rd Edition in 2 vols. 1919. (New Edn. Vol. 1, 1924.)
- L.—The Lancet, London.
- L.H.—Pharmacopœia of the London Hospital, 1925 and earlier Edns.
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* In connection with a text heading signifies that the name which it precedes is a British Registered Trade Mark, *e.g.*, *Exalgine. The * is only applied to the principal heading and is not repeated throughout the book.

INTERNATIONAL (1925) ATOMIC WEIGHTS AND ATOMIC NUMBERS.

	Sym- bol.	At. Num- ber.	At. Weight.		Sym- bol.	At. Num- ber.	At. Weight.
Silver ..	Ag	47	107.880	Nitrogen ..	N	7	14.008
Aluminium ..	Al	13	26.97	Sodium ..	Na	11	22.997
Argon ..	A (Ar)	18	39.91	Columbium.	Cb	} 41	93.1
Arsenic ..	As	33	74.96	Niobium ..	Nb		
Gold ..	Au	79	197.2	Neodymium	Nd	60	144.27
Boron ..	B	5	10.82	Neon ..	Ne	10	20.2
Barium ..	Ba	56	137.37	Nickel ..	Ni	28	58.69
Beryllium ..	Be	} 4	9.02	Oxygen ..	O	8	16.000
Glucinium ..	Gl			Osmium ..	Os	76	190.8
Bismuth ..	Bi	83	209.00	Phosphorus	P	15	31.027
Bromine ..	Br	35	79.916	Lead ..	Pb	82	207.20
Carbon ..	C	6	12.000	Palladium..	Pd	46	106.7
Calcium ..	Ca	20	40.07	Praseody- mium	Pr	59	140.92
Cadmium ..	Cd	48	112.41	Platinum ..	Pt	78	195.23
Cerium ..	Ce	58	140.25	Radium ..	Ra	88	225.95
Chlorine ..	Cl	17	35.457	Rubidium .	Rb	37	85.44
Cobalt ..	Co	27	58.94	Rhodium ..	Rh	45	102.91
Chromium ..	Cr	24	52.01	Radon ..	Rn	86	222.
Caesium ..	Cs	55	132.81	Ruthenium..	Ru	44	101.7
Copper ..	Cu	29	63.57	Sulphur ..	S	16	32.064
Dysprosium..	Dy	66	162.52	Antimony .	Sb	51	121.77
Erbium ..	Er	68	167.7	Scandium ..	Sc	21	45.10
Europium ..	Eu	63	152.0	Selenium ..	Se	34	79.2
Fluorine ..	F	9	19.00	Silicon ..	Si	14	28.06
Iron ..	Fe	26	55.84	Samarium..	Sm	62	150.43
Gallium ..	Ga	31	69.72	Tin ..	Sn	50	118.70
Gadolinium .	Gd	64	157.26	Strontium..	Sr	38	87.63
Germanium .	Ge	32	72.60	Tantalum ..	Ta	73	181.5
Hydrogen ..	H	1	1.008	Terbium ..	Tb	65	159.2
Helium ..	He	2	4.00	Tellurium..	Te	52	127.5
Mercury ..	Hg	80	200.61	Thorium ..	Th	90	232.15
Holmium ..	Ho	67	163.4	Titanium ..	Ti	22	48.1
Iodine ..	I (J)	53	126.932	Thallium ..	Tl	81	204.39
Indium ..	In	49	114.8	Thulium ..	Tm	69	169.4
Iridium ..	Ir	77	193.1	Uranium ..	U	92	238.17
Potassium ..	K	19	39.096	Vanadium..	V	23	50.96
Krypton ..	Kr	36	82.9	Tungsten ..	} W	74	184.0
Lanthanum .	La	57	138.90	Wolfram ..			
Lithium ..	Li	3	6.940	Xenon ..	Xe	54	130.2
Lutecium ..	Lu	71	175.0	Yttrium ..	Y	39	88.9
Magnesium..	Mg	12	24.32	Ytterbium..	Yb	70	173.6
Manganese. .	Mn	25	54.93	Zinc ..	Zn	30	65.38
Molyb- denum ..	Mo	42	96.0	Zirconium..	Zr	40	91

See also *International Table of the Radio-active Elements and their constants*, p. 327 et seq. and pp. 352 and 353.

INTERNATIONAL TABLE OF ISOTOPES (1923)

Contrary to the Atomic Theory of Dalton that atoms of the same element are similar to one another and equal in weight, the view now is that there must exist elements having chemical properties identical for all practical purposes but the atoms of which have different weights.

ATOMIC NUMBER.—A *chemical element* is defined by its *atomic number*. This number represents the excess of positive over negative charges in the constitution of the atomic nucleus; theoretically the *atomic number* represents also the number of electrons which rotate round the central positive nucleus of the atom. Each *atomic number* also represents the place occupied by the element in the Mendeleef Table.

Various methods have been suggested to determine the *atomic numbers*, e.g., by deducing them from the wave-lengths of the high frequency spectra by applying Moseley's law.

ELEMENTS (SIMPLE AND COMPLEX). ISOTOPES.—If the above definition is accepted, each chemical element may be *simple* or *complex*, according as its atoms are all of equal mass or not.

In the latter case, the element consists of as many *isotopes* as its atoms have different masses. A *complex* element is a *mixture of isotopes*. Three methods (J. J. THOMSON, ASTON, DEMPSTER) have been devised to determine isotopes. The most important is that of ASTON.

NOTATION.—The elements, simple or complex, are represented by the ordinary symbols. To indicate any particular isotope its atomic mass (*l*) is written as an index to the right of the symbol representing the mixture. Thus, Cl^{35} indicates the isotope of chlorine having an atomic mass 35. This number represents the relative mass of its atom, the atom of oxygen (a simple element) being taken as 16.

ELEMENTS INCLUDED IN THE TABLE.—The isotopes of lead which are the ultimate result of disintegration of radioactive Elements, and the radioactive isotopes only appear in the International Table of the radioactive Elements, pp. 327-330. Only those elements appear in the Table of Isotopes which are recognised as simple, or are complex elements whose isotopes have been determined with sufficient certainty.

PROVISIONAL VALUES are shown by numbers in brackets.

"ATOMIC MASS."—This expression is reserved for isotopes of simple elements considered from the isotopic point of view. The expression *atomic weight* retains its usual meaning, and is applied to elements without consideration of their isotopic constitution.

The atom remains the smallest portion of an element to be involved in chemical changes, though this is not to say that it is indivisible.

The diameter of an atom is estimated as of the order of 10^{-8} cm., and that of an electron as 10^{-13} cm.,—J. Patrick, *P.J.* i. 28, 105.

TABLE OF ISOTOPES.

(INTERNATIONAL, 1923).

Element.	Atomic number	Atomic weight(1)	Minimum Number of Isotopes.	Masses of Isotopes (2).	% accuracy.	Observer.	Reference.
H	1	1.008	1	1.008	0.2	A.	3; 5
He	2	4.00	1	4	0.2	A.	3; 5
Li	3	6.94	2	7; 6		A., T., D.	9; 10; 14; 16
Gl	4	9.1	1	9		T.	17
B	5	10.9	2	11; 10	0.1	A.	6; 7
C	6	12.005	1	12		A.	2; 5
N	7	14.008	1	14	0.2	A.	3; 5
O	8	16.000	1	16		A.	2; 5
F	9	19.0	1	19	0.1	A.	6; 7
Ne	10	20.2	2	20; 22	0.1	A.	1; 4; 5
Na	11	23.00	1	23		A.	11; 14
Mg	12	24.32	3	24; 25; 26		D.	15; 16
Al	13	27.0	1	27		A.	21
Si	14	28.1	2	28; 29; (30)	0.1	A.	6; 7
P	15	31.04	1	31	0.2	A.	6; 7
S	16	32.06	1	32	0.2	A.	6; 7
Cl	17	35.46	2	35; 37	0.1	A.	2; 5; 13
A	18	39.9	2	40; 36	0.1	A.	3; 5; 8
K	19	39.10	2	39; 41		A.	11; 14
Ca	20	40.07	(2)	40; (44)		D.	18
Fe	26	55.84	(1)	56; (54)?	see refer.	A.	19
Ni	28	58.68	2	58; 60	0.1	A.	12
Zn	30	65.37	4	64; 66; 68; 70		D.	18
As	33	74.96	1	75	0.1	A.	6; 7
Se	34	79.2	6	80; 78; 76; 82; 77; 74;	0.1	A.	21
Br	35	79.92	2	79; 81	0.1	A.	6; 7
Kr	36	82.92	6	84; 86; 82; 83; 80; 78	0.1	A.	3; 5
Rb	37	85.45	2	85; 87		A.	11; 14
Sn	50	118.7	7 (8)	120; 118; 116; 124; 119; 117; 122; (121)	sec refer.	A.	20
I	53	126.92	1	127	0.2	A.	8; 13
Xe	54	130.2	7 (9)	129; 132; 131; 134; 136; 128; 130; (126); (124)	0.1	A.	3; 5; 8; 13; 21
Cs	55	132.81	1	133		A.	11; 14
Hg	80	200.6	(6)	(197-200); 202; 204	0.1	A.	2; 3; 5

1. *Nature*, November 27, 1919.
2. *Nature*, December 18, 1919.
3. *Nature*, March 4, 1920.
4. *Philosophical Mag.*, April, 1920.
5. *Philosophical Mag.*, May, 1920.
6. *Nature*, July 1, 1920.
7. *Phil. Mag.*, Nov., 1920.
8. *Nature*, December 9, 1920.
9. ASTON and THOMSON, *Nature*, Feb., 24, 1921.
10. DEMPSTER, *Science*, Ap. 15, 1921.
11. ASTON, *Nature*, March 17, 1921.
12. ASTON, *Nature*, June 23, 1921.
13. ASTON, *Phil. Mag.*, July, 1921.
14. ASTON, *Phil. Mag.*, Sept., 1921.
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16. DEMPSTER, *Phys. Review*, Dec. 21.
17. G. P. THOMSON, *Phil. Mag.*, Nov., 1921.
18. DEMPSTER, *Phys. Review*, 19; p. 431; 1922.
19. ASTON, *Nature*, Sept. 2, 1922.
20. ASTON, *Nature*, June 24, 1922.
21. ASTON, *Nature*, Nov. 18, 1922.

Observers : A=ASTON, D=DEMPSTER, T=THOMSON (G. P.)

(1) International Values for 1922.

(2) In order of intensity of spectral bands.

Iron, Copper, Silver, and Antimony have each 2 isotopes, and Magnesium, Silicon and Sulphur have each 3 isotopes.—J. Patrick, P.J. i./28, 105.

For a recent comprehensive table see F. W. Aston, B.J.R., Jan., '28.

Suggested International Atomic Weights for Pharmaceutical Purposes.

(From a paper by W.H.M., read at an Evening Meeting of the Pharmaceutical Society of Great Britain, in London.—P.J. i./II, 170, 178.)

Aluminium	27	Lithium	7
Antimony	120	Magnesium	24
Arsenic	75	Manganese	55
Barium	137	Mercury	200
Bismuth	208	Nitrogen	14
Boron	11	Oxygen	16
Bromine	80	Phosphorus	31
Calcium	40	Platinum	195
Carbon	12	Potassium	39
Cerium	140	Silicon	28
Chlorine	35.5	Silver	108
Chromium	52	Sodium	23
Copper	63.5	Strontium	88
Gold	197	Sulphur	32
Hydrogen	1	Tin	119
Iodine	127	Zinc	65
Iron	56	Thorium	232
Lead	207		

The Structure of the Atom.

It is now generally accepted that the atoms of the elements all have the same type of structure, consisting of a positively charged central nucleus of minute dimensions, responsible for most of the mass of the atom, surrounded by electrons which occupy, rather than fill, a much larger region. This has a diameter of the order of 2×10^{-8} Cm. The results of radioactive change, and also the liberation of Hydrogen atoms from Boron, Fluorine, Sodium, Nitrogen, Aluminium and Phosphorus, by bombardment with α particles, lead to the general view that all atoms contain complex nuclei built up of Hydrogen and Helium nuclei and electrons. If, as is generally supposed, Helium itself is composed of four Hydrogen nuclei and two electrons, it seems probable that the nuclei of all atoms consist ultimately of Hydrogen nuclei, or "protons" with the addition of negative electrons.

The resultant nuclear charge in an atom is proportional to its atomic number and varies from 1 in the case of Hydrogen, to 92 with Uranium, and these also represent the number of planetary electrons surrounding the small nucleus. The physical and chemical properties of the elements are decided by the number and arrangement of the external electrons, and these are governed by the nuclear charge, the mass having only a secondary effect. This hypothesis readily explains the existence of isotopes, which are atoms having the same nuclear charge but different masses (E. Rutherford, J.C.S.T. '22,400).

Physicists differ in their conception of the manner in which the

electrons are grouped round the positive nucleus. J. J. Thomson (1904) deduced that the electrons would form certain ring systems, according to the number present, the periodic recurrence of similar rings accounting for the periodicity of properties of the elements.

Bohr (1913) also regards the electrons as circulating round a nucleus, but assumes they "jump" from one orbit to another, causing radiation. In the case of Hydrogen, calculations agree very well with spectral results, but are unsatisfactory with complicated atoms. (For other views *v.* Recent Advanc. Physicl. and Inorgan. Chem.—Stewart).

The Langmuir-Lewis Octet Theory differs from the majority in being based on the chemical behaviour of the elements. It is suggested that the external electrons, which determine the valency of the atom, in most cases tend to form "octets," that is become arranged in space at the angles of a cube. Two atoms unite to form stable groups of electrons, either by transferring electrons from one atom to another, or else by sharing electrons. In the former case the atoms are left oppositely charged but held together by electrostatic forces, $\text{Na} + \text{Cl} -$ being an example of electrovalency, whereas in the second case the valency is non-polar, *e.g.* $\text{Cl} - \text{Cl}$, and is called a covalency. This theory has been extended by Lowry to apply to organic compounds. (*v.* J.C.S.T. '23, 831).

The Structure of the Atom.—N. Bohr, *Na.*, 112, '23, 29.

According to Rutherford's researches, the atom is built up of particles of $+$ and $-$ electricity, arranged in an orderly way, which the work of Bohr has done much to reveal. Moseley forms a new order for the elements in atomic number, revealing a relation of great simplicity. The nuclear atom postulates one consisting of an extremely dense nucleus of $+$ electricity surrounded by a planetary system of $-$ charged electrons. Hydrogen nuclei no doubt form the essential constituents of the nuclear structure, which in the case of a heavy atom is probably a very complex system.—J.R.S., Oct. '23.

Although the Hydrogen atom has only one electron, it may have alternative orbits. Radiation, according to Bohr, is emitted when the electron drops from one possible orbit to another, and not otherwise. Moseley's work showed that the atoms of chemical elements step by equal differences, in regular arithmetical progression, from the lowest to the highest, and assuming a nuclear constitution Moseley concluded that the step each time must be the addition of a positive charge to the nucleus.—Sir Oliver Lodge, J.R.S., Jan. '24, p. 10.

The relation in size of an electron to an atom is as 1 to 100,000. Positive ray analysis explained, with its application to isotopes, and mention is made to Sir W. Braggs' work on crystal structure.—F. Browne, P.J. ii./21, 4.

The method of determining the number and individual weights of isotopes in any given element, consists in ionisation of the substance in a discharge tube, the rays then being bent by a magnet and caused to pass through two slits and then through an electric spectrum, and the spectra photographed. The weights of the isotopes determined by this method were always whole numbers.—C.D., April 16/21, 42.

PERIODIC TABLE OF ELEMENTS FOUNDED ON THAT OF MENDELEEFF (1915 Atomic Weights—*purposely retained*.)

Zero Group.	Group I.	Group II.	Group III.	Group IV.	Group V.	Group VI.	Group VII.	Group VIII.
<i>x</i>								
<i>y</i>	H = 1.008							
He = 3.99	Li = 6.94	Gl(Be) = 9.1	B = 11	C = 12	N = 14.01	O = 16	F = 19	
Ne = 20.2	Na = 23	Mg = 24.32	Al = 27.1	Si = 28.3	P = 31.04	S = 32.07	Cl = 35.46	
A = 39.88	K = 39.1	Ca = 40.07	Sc = 44.1	Ti = 48.1	V = 51	Cr = 52	Mn = 54.93	Fe = 55.84 Co = 58.97 Ni = 58.68
	Cu = 63.57	Zn = 65.37	Ga = 69.9	Ge = 72.5	As = 74.96	Se = 79.2	Br = 79.92	
Kr = 82.92	Rb = 85.45	Sr = 87.63	Yt = 89	Zr = 90.6	Cb = 93.5	Mo = 96		Ru = 101.7 Rh = 102.9 Pd = 106.7
	Ag = 107.88	Cd = 112.4	In = 114.8	Sn = 119	Sb = 120.2	Te = 127.5	I = 126.92	
Xe = 130.2	Cs = 132.81	Ba = 137.37	La = 139	Ce = 140.25				
	Au = 197.2	Hg = 200.6	Yb = 172	Pb = 207.1	Ta = 181.5	W = 184		Os = 190.9 Ir = 193.1 Pt = 195.2
		Ra = 226.4	Tl = 204	Th = 232.4	Bi = 208	U = 238.5		

In an Appendix to "The Principles of Chemistry, 1905," Mendeléeff included the elements of the Argon group and Radium, and found places in addition for two hypothetical elements which he placed before Helium and designated *x* and *y*. *y* is supposed to be an analogue of Helium and may be identified hereafter with "Coronium," which has been recognised in the Sun's coronal atmosphere. This gas according to Mendeléeff would have density about 0.2 and therefore, molecular weight 0.4 or about $\frac{1}{16}$ that of Helium.

x is the 'Ether' for which Mendeléeff supposes a molecular structure. It is assumed to be inert like the Argon group and to possess a low density and Atomic Weight estimated at 0.000,000,000,053.—Mendeléeff Memorial Lecture.—Tilden, "Nature," 3/2/10, p. 416.

An element with the atomic weight 3 has been found by J. J. Thomson—? some allotropic variety of Hydrogen analogous with Ozone and Oxygen. An element with this weight had been predicted by Mendeléeff, who endowed it with super-fluorine properties.—P.J. i./13, 101.

POISONS SCHEDULE.

DAINGEROUS DRUGS (CONSOLIDATED) REGULATIONS, 1928.

These Regulations consolidate into one code the Regulations 1921-1928. under the 1920 Act and bring into Part III. of that Act ***Extract and Tincture of Indian hemp, Dihydro-oxycodone*** (Eucodal or Eukodol), ***Dihydrocodone*** (Dicodide or Dicodid) and preparations containing them, and preparations containing ***less than one tenth per cent of diacetyl morphine.***—P.J. ii./28,450.

D.D. Act 1920 re Manufacture, Sale, etc., of Benzoyl Morphine.—P.J. ii./28,528.

D.D. (Consolidated) Regulations 1928 as to retail sale to the public of Coca leaves and preparations containing less than 0.1% of Heroin effective from Jan. 1, 1929.—P.J. ii./28,604.

Esters of morphine and their respective salts and any preparation, admixture, and extract containing any of the said esters added to Part III of the D.D.A., 1920.—Aug. 20th, 1929.

APPROXIMATE EQUIVALENT WEIGHTS.

WEIGHTS. IMPERIAL TO METRIC.

grain.	Gm.	grain.	Gm.	grains.	Gm.
$\frac{1}{1000}$	= 0.000065	$\frac{1}{4}$	= 0.016	15	= 1.0
$\frac{1}{200}$	= 0.0003	$\frac{1}{8}$	= 0.02	20	= 1.2
$\frac{1}{100}$	= 0.0006	$\frac{1}{2}$	= 0.03	30	= 2.0
$\frac{1}{64}$	= 0.001	$\frac{3}{4}$	= 0.05	45	= 3.0
$\frac{1}{50}$	= 0.0013	1	= 0.06	60	= 4.0
$\frac{1}{40}$	= 0.0015	(Strictly 0.06479)		90	= 6.0
$\frac{1}{32}$	= 0.002	grains		120	= 8.0
$\frac{1}{25}$	= 0.0025	$1\frac{1}{2}$	= 0.1	150	= 10.0
$\frac{1}{20}$	= 0.003	2	= 0.12	180	= 12.0
$\frac{1}{16}$	= 0.004	3	= 0.2	$\frac{1}{2}$ ounce	
$\frac{1}{12}$	= 0.005	4	= 0.25	(av.)=	15.0
$\frac{1}{10}$	= 0.006	5	= 0.3	1,,	= 30.0
$\frac{1}{8}$	= 0.008	6	= 0.4	(or nearer	28.35.
$\frac{1}{6}$	= 0.01	8	= 0.5	1 pound	
$\frac{1}{5}$	= 0.012	10	= 0.6		= 453.59
		12	= 0.8		

WEIGHTS. METRIC TO IMPERIAL.

1 kilogramme	= 2 lb.	$3\frac{1}{4}$ oz.
500 Gm.	= 1,,	$1\frac{5}{8}$,,
100,,	= $3\frac{1}{2}$ oz.	
25,,	= $\frac{7}{8}$,,	
10,,	= $\frac{1}{3}$,,	
1,,	= 15.4324 grains.	
$\frac{1}{2}$,,	or 500 milligrammes	= 7.7,,	

MEASURES. IMPERIAL TO METRIC.

minim.	Cc.	minims.	Cc.	fluid oz.	Cc.
$\frac{1}{2}$	= 0.03	15	= 1.0	1	= 30.0
1	= 0.06	20	= 1.2	fluid ozs.	
minims.		25	= 1.5	2	= 60.0
2	= 0.12	30	= 2.0	4	= 115.0
3	= 0.2	40	= 2.5	5	= 140.0
4	= 0.25	45	= 3.0	6	= 170.0
5	= 0.30	60	= 4.0	8	= 230.0
6	= 0.4	90	= 6.0	10	= 280.0
8	= 0.5	120	= 8.0	20	= 563.0
10	= 0.6	240	= 15.0	gallon	litres.
12	= 0.8			1	= 4.536

MEASURES. METRIC TO IMPERIAL.

1 Cc.	= 15 (nearer 17) minims.
1 litre	= 1 pint 15 fl. oz. approx.

MEASURES OF LENGTH.

1 micromillimetre	=	$\frac{1}{1000000}$ millimetre, usually represented by $\mu\mu$.
1 micron	=	$\frac{1}{1000}$ millimetre, or 1 micrometre, ,, ,, μ .
1 millimetre	=	0.03937 inch.
1 centimetre	=	0.3937 inch.
1 decimetre	=	3.937 inches.
1 metre	=	39.370113 inches or 1 yard 3.37 inches nearly.

ANALYTICAL ADDENDA TO CHEMICALS & MATERIA MEDICA IN VOL. I.

ACACIÆ GUMMI (B.P.'14).

Impurities and fraudulent additions.—

Gum Acacia must be free from Starch, Dextrin, Sugars and Tannin. Ash limit (B.P.'14) not to exceed 4%.

Kordofan Gum contains 12 to 15% moisture, while Gum Senegal contains rather more. If the amount exceeds 20%, the gum, instead of being brittle, is tough and difficult to grind to powder.

The optical rotation of good gum is usually slightly lævorotatory.

Acidity of Gum Acacia.—

All the samples we have examined were found to give an acid solution, the amount of Sodium Hydroxide required to neutralise 1000 Gm. of Gum varying from 2.48 to 3.2 Gm., giving an average of 2.84 Gm. The clarity of the solutions is in no way related to its reaction.

A sample of Mucilage two months old showed that in a sterile solution (this having been preserved with Benzoic Acid), relatively no hydrolysis of the component salts had occurred.

The *Straining of Mucilage* can be effected by forcing it through muslin by air expansion. A bottle about half full of Mucilage is tied lightly over the neck with muslin, thoroughly cooled, and then on bringing into a warm situation and inverting, the Mucilage will be forced through. When it ceases to drop, the process of alternate heating and cooling is repeated. To obtain an absolutely bright Mucilage the process might be reversed, making the bottle (above)—previously heated—the receiver.—P.J. ii./09, 6.

The function of Gum in official Acacias is no doubt to preserve the moisture necessary to keep the plants alive during the months of drought—December to April. The cicatrisation of the wounds, in collecting, is of secondary importance, the gum being exuded only during periods of extreme dryness, the process stopping with the slightest rain.—E. Perrot, P.J. ii./20, 510.

100 tons of Gum Acacia stated to be available annually in the forests of Argentina.—Jl. Am. Ph. A., '20/1118.

Sheep poisoned and killed by eating the pods of *Robinia pseud-acacia*, the common garden "acacia" tree.—P.J. i./23, 263.

ACETANILIDUM (B.P. '14).

Tests for Recognition.—See 'Scheme for Recognition of Organic Chemicals.'

Estimation.—Hydrolyse 1.5 Gm. by boiling for 15 mins. with 50 Cc. of 20% Hydrochloric Acid and dilute to 500 Cc. To 25 Cc. of this solution add excess standard potassium bromide-bromate solution to precipitate tribromoaniline, and estimate excess bromine in the usual way.—J.C.S.A. ii./1921, 604.

Toxicology.—Danger of Acetanilide as headache powders.—Dixon, P.J. ii./12, 555. When first introduced, two 5 grain doses at some hours' interval produced cyanosis.—L. ii./10, 575. See also L. i./13, 1491. Earlier refs. in Edn. xvii.

Toxicological studies of acetanilide poisoning.—A. G. Young and J. A. Wilson, Jl. Ph. and Exp. Ther., Mar. '26, 133.

Effect of other drugs on toxicity of Acetanilide:—

Sodium Bicarbonate has power in combating its toxic effects. It probably prevents the whole dose of the drug entering at once into the blood. The toxicity of acetanilide is increased by Caffeine, Codeine and Morphine.

Acetanilide and Methylene Blue Tubes are used as pyrometers for testing the efficacy of sterilisers. See *Sterilisation chapter*.

ACIDUM BENZOICUM (B.P. '14).

Tests.—Should not develop odour of benzaldehyde when warmed with its own weight of potassium permanganate and ten times its weight of dilute sulphuric acid (B.P. '14 test for cinnamic acid). Solution in sulphuric acid when gently warmed should not turn darker than light yellow.—U.S. M.Pt. 120—122° C.

Use as Preservative—The Acid and Sodium Benzoate are not harmful if used in moderate amount. 0.1% is sufficient to preserve meat and butter. 0.05% is sufficient for fruit and fruit syrups.

See however Preservatives in Food Regulations.

The antiseptic effect of Benzoic Acid in the small concentrations permitted is relatively low, and the resistance of yeasts varies within wide limits—the activity of some being suppressed by 0.03—0.05% while others resist 0.07—0.1%. A new yeast discovered in pear-juice, *Saccharomyces Lousohnienis*, resists 0.1% Sodium Benzoate in glass vessels and 0.15% in presence of wood particles. It is killed at 65° C.—per Y.B.P./26,329.

Detection in Foodstuffs.—Extract with a mixture of ether and petroleum ether in equal parts; this evaporated may contain saccharin (taste), salicylic acid (by its colour with ferric chloride), and benzoic acid—recognised by odour, crystalline form, and conversion into aniline blue by heating with Rosaniline and Aniline. This is Triphenyl-Rosaniline, $C_{33}H_{33}N_3O = 547.288$ or $C_{20}H_{11}(C_6H_5)_3N_3 = 529.272$. Its Hydrochloride is called **Opal Blue**, *Syn. Spirit Blue*, being soluble in spirit.

Water-Soluble-Blue is obtained by converting Spirit Blue (above mentioned) into Triphenyl-Rosaniline-Trisulphonic Acid by treatment with Sulphuric Acid, and is usually supplied as the Ammonium Salt. (Simpson.)

Nicholson's Blue, Syn. Alkali Blue, is the Sodium Salt of Triphenyl-Rosaniline-Monosulphonic Acid made by sulphonating Spirit Blue, almost in the cold.

(Nicholson's Blue is dyed on wool or silk from a slightly alkaline or neutral bath. The goods are washed and then developed in a bath acidulated with Sulphuric Acid. The ordinary water-soluble blues dye from an acid bath.)

Determination in Foodstuffs (Fruits and Vegetables), in permitted amounts, specified under the Regulations in force since Jan. 1, 1927. Report No. 39 on "Public Health and Medical Subjects" (Min. Health), by G. W. Monier-Williams. This is a lengthy process, starting with steam distillation, after saturating if necessary with salt, and subliming in presence of sand for 1 to 1½ hours at 160° C., and ultimately weighing the Benzoic Acid present.—Y.B.P./27,182.

Various methods of estimation of Benzoates and Salicylates.—E. B. R. Prideaux and A. O. Bentley.—P.J. i./23,427.

A distillation method of determination in foods (butter, margarine, and egg products) and in wines (not sweet).—per Y.B.P.'27,183. Also an adaptation of the French Official method for detection in wines, showing 1 mgr. in 100 Cc. wine.—*ibid.*'25,149.

COLORIMETRIC ESTIMATION in cordials, etc. The Aniline Blue reaction is unsatisfactory, as Acetic, Succinic and Salicylic Acids also give the reaction. Best results with a modification of Halphen's Reaction, Hydroxylamine Hydrochloride being employed as reducing agent. Presence of Benzoic Acid indicated by fine red colour.—A. J. Jones, B.P. Conf., '25, per Y.B.P.'25,493.

Caution needed in search for traces of preservatives in Caramel and boiled sugar sweets, which yield a crystalline acid substance (m.pt. 122° C.), giving a violet colour with Ferric Chloride, similar to Benzoic Acid.—per Y.B.P., '27,185.

Siam Benzoin.

The only source of Siam Benzoin of commerce is *Styrax Tonkinense*, Craib. found in the district between Luang Prabang and Hanoi. *S. Benzoides* of N. W. Siam yields a fragrant resin, but it is not certain that it enters commerce. The method of preparation with hog's marrow would account for the characteristic appearance of Siam Benzoin.—E. M. Holmes, P.J. ii./13, 802,804. *See also* P.J. i./07,127; ii./12,777.

Siam Benzoin consists essentially of crystalline Coniferyl Benzoate with

free Benzoic Acid and *d*-siarresinolic Acid. Slow oxidation of Coniferyl Benzoate yields a small amount of Vanillin. Siam Benzoin is readily saponifiable. It is a pathological product of the plant.—per Y.B.P.'26,147.

Unlike the Sumatra variety, it contains practically no Cinnamic Acid.

Friars' Balsam.

Fryer's Balsam or Jesuits' Drops were mentioned as early as 1725 by Pomet. For further historical notes see *Edn. XVIII., Vol. II., p. 2.*

ACIDUM BORICUM (B.P. '14).

Boron has an abnormal value in its temperature co-efficient of resistance. A small piece of fused Boron mounted in series with an electric lamp obstructs nearly all the current, but on warming the Boron the resistance is reduced and the lamp lights. A filament of Boron at ordinary temperatures will show a resistance of 5,620,000 ohms, but when warmed to a dull red heat the resistance drops to 5 ohms. A splinter of Boron is almost as hard as a diamond. It will easily scratch the very hard substance Carborundum.

Lead as impurity in Boric Acid is of importance. B.P. '14 limit is 25 parts per million.

Detection of Boric Acid. See also Milk Analysis.

Boron compounds exist as normal constituents in Cacao and Cacao products in appreciable amounts—0.01% in chocolate, expressed as Boric Acid, and from 0.0217 to 0.0837% in commercial samples of Cacao Beans and Cocoa. They also occur in small quantities (0.01%) in coffee beans. Samples of seaweed—Irish Moss, Seaweed (*Fucus*) and Agar-agar also contain traces, apparently as normal constituents.—per Y.B.P./27,165. Also beans.—*ibid.*, '26,181.

Tincture of Mimosa Flowers made by warm maceration (10 minutes on water bath) of 5 Gm. first in 50 Cc., and then with 40 Cc. Alcohol 95% after decanting, used for finding minute traces.—For details *vide* P.J. i./14,31.

Moisten Congo Red paper with a saturated aqueous solution and dry over a small flame: a blue colour is gradually developed. By using 1 in 1000 solution of Congo Red in a capsule and adding a little of a Boric Acid solution the presence of 0.00001 Gm. may be detected. The test is best applied to Methyl or Ethyl Boric ester obtained by distillation.—per Y.B.P.'25,138.

The solution suspected to contain a borate is made slightly alkaline with sodium hydroxide and evaporated practically to dryness. The residue is treated with 1 Cc. of concentrated sulphuric acid and cooled. Two Cc. of Methyl Alcohol are added and the mixture is transferred to a test tube fitted with a rubber stopper and two glass tubes. One of these extending to the bottom is bent at right angles and acts as a mouthpiece. The other conducts the vapours and is also bent, but drawn to a long capillary at least 3 cm. long and not more than 0.5 mm. bore. When air is blown through the apparatus the bubbles rising through the heated solution convey volatile methyl borate (if present), which tints a small Bunsen flame a characteristic green colour.—A. Gabriel and H. G. Tanner, *Jl. Am. Chem. Soc.*, per C.D. ii./28,777.

We find the test satisfactory for 0.2 mgr. Boric Acid.

Manna can replace Glycerin in the titration of Boric Acid.—L. E. Iles, *Analyst*, 1918, 43, 323.

Glycerinum Acidi Borici.

The reaction between Boric Acid and Glycerin leads, it is thought, to the formation of Glycerol-Boric Acid, a mono-basic acid with formula:—



Sodii Biboras. Borax.

Arsenic B.P. '14 limit is 5 parts per million. Lead the same.

The discovery in 1926 of enormous deposits of Kernite (or Rasorite), an entirely new mineral, in the Mohave Desert, Kern County, California, will probably give the U.S.A. a complete monopoly in the mining of borates. Kernite is virtually pure Sodium Borate, containing over 75% pure mineral with 25% clay. For marketing, it is only necessary to dissolve in water, filter off the clay and recrystallise. Owing to the fact that 6 mols. of water are added to Kernite in the refining process to bring it up to commercial Sodium Borate (which contains 10 mols.), one ton of Kernite makes nearly a ton and a half of Borax.—*Am. Jl. Pharm.*, July '28, 480.

French method recommended for testing Official Borax and other substances containing borates. Dissolve 1.91 Gm. of sample, finely powdered, by warming on water-bath in 25 Cc. water and 50 Cc. Glycerin : solution complete in 30 minutes. When quite cold, titrate with N/NaOH with Phenolphthalein indicator. If pure, it will require exactly 10 Cc. N/NaOH solution.—per Y.B.P.'27,329.

Sodium Perborate is stated to contain "10% active oxygen." This can be calculated as follows:—

$2 \text{NaBO}_3 \cdot 4\text{H}_2\text{O} = \text{Na}_2\text{B}_2\text{O}_4 + \text{O}_2 + 4\text{H}_2\text{O}$, i.e., 310 approx. Sodium Perborate should produce 32 available Oxygen=10% approx. allowing for impurity.

Assay (Fr. Cx. Supp. II.).—Dissolve 0.25 Gm. of the salt in 50 Cc. of distilled water and 10 Cc. of dilute Sulphuric Acid. Add to this solution sufficient solution of Potassium Permanganate (3.16 : 1000) to produce a permanent rose colour. For this purpose at least 28 Cc. should be required, corresponding to 9% of active oxygen, or 86.5% for the pure salt.

Estimation of available oxygen in the Perborate and in Perborate Soap Powders. A volumetric method based on the reaction $\text{NaBO}_3 + \text{CaOCl}_2 + \text{H}_2\text{O} = \text{NaH}_2\text{BO}_3 + \text{CaCl}_2 + \text{O}_2$ found best.—H. Trickett, C.D. '20,283.

ACIDUM CARBOLICUM (B.P. '14).

Quantitative Estimation of Phenol.—This may be effected by converting it into Tribromophenol $\text{C}_6\text{H}_2\text{Br}_3\text{OH}$:—

Dissolve Phenol 1.567 Gm. in water sufficient to make 1000 Cc. Place 25 Cc. of the Solution in a 200 Cc. stoppered bottle, add 30 Cc. of N/10 Bromine Solution (**Koppeschaar's Solution**) and shake repeatedly for half an hour, then add 5 Cc. of 20% Potassium Iodide Solution, shake well, add 1 Cc. Chloroform and titrate excess of Iodine with N/10 Thiosulphate. Subtract the number of Cc. required from thirty: the remainder equals the number of Cc. N/10 Bromine used up. This multiplied by 4 gives the percentage of absolute Phenol (i.e., 1 Cc. N/10 Br.=0.00156747 Gm. Phenol).

The process works satisfactorily,—we obtained with a sample of detached crystals (M.Pt. 41° C.), 98% as an average of three determinations.

Koppeschaar's Bromine Solution is made as follows:—

Dissolve Potassium Bromate 3.2 Gm. and Potassium Bromide 50 Gm. in Water 900 Cc. To standardise place 20 Cc. in a 250 Cc. bottle with Water 75 Cc. and 5 Cc. Pure Hydrochloric Acid. Shake a few times, quickly introduce 5 Cc. of 20% Potassium Iodide Solution and titrate the Iodine set free by N/10 Sodium Thiosulphate. Dilute the Bromine Solution so that equal volumes of it and the N/10 Thiosulphate exactly correspond in the conditions of the test.—cf., U.S. X., p. 498.

Excretion of Phenol after poisoning by.—Dublin Jl. Med. Sci., May, 1914. L. ii./14,1585.

Bad effects from Compresses, local use and excessive inhalation.

Compresses soaked with 5% solution of Phenol may cause coma.—L. i./95, 1362. Even 1 in 40 has caused carboluria and death when applied to penis after circumcision.—W. W. W. cf. L. i./09,564—but this is exceptional. Danger when used as dressings to extremities—fingers and toes—L. i./03,1099. B.M.J. i./07,1110. P.J. ii./11,780.

Ochronosis associated with carboluria caused by local application of Carbolic Oil 1 in 20.—Q. Jl. Med., July, 1910.

Inhalation of fumes of Carbolic Acid, owing to dropping of a Winchester and the boy starting to mop it up with a cloth, caused grave poisoning symptoms. Intravenous Saline 2 pints with addition of 2 drachms of Sodium Bicarbonate saved life. Breathing (assisted by the use of Oxygen) improved at once.—R. Eccles Smith, L. ii./22,1359.

Absorption of crude Carbolic Acid through the skin with fatal result. A bottle broke in a man's pocket on his journey home by train—extensive burning of hip, thigh and scrotum. Ultimate death.—W. R. M. Turtle and T. Dolan, L. ii./22,1273.

Carbolic Acid Ointment. 5% of lard instead of the equivalent amount of Soft Paraffin, prevented crystals separating.—J. H. Franklin, P.J. ii./24,656.

ACIDUM CRESYLICUM (B.P. '14).

The content in the Phenol-Cresol Fraction (185° to 195° and 195° to 205°) and the High Boiling Fraction (205°—250° and 250° upwards) vary within wide limits commercially.

We have combined some figures obtained by Evans with a fractionation of our own (Source M in the table) :—

Source.	Description.	Phenol-Cresol Fraction.				High-Boiling Fraction.		Residuum
		(a) Below 185°.	(b) 185°— 195°.	(c) 195°— 205°.	Total (b) + (c).	205°— 250°.	250° Up.	
		Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Pr. Ct.
A	Pallid.	$\frac{1}{2}$	71	24 $\frac{1}{2}$	95 $\frac{1}{2}$	—	—	4
B	"	1	35	43	78	14(220°)	—	7
C	Crude	3 $\frac{1}{2}$	1	4 $\frac{1}{2}$	5 $\frac{1}{2}$	44	22(330°)	25
C	"	4 $\frac{1}{2}$	2 $\frac{1}{2}$	6	8 $\frac{1}{2}$	50(270°)	—	37
C	Nigrum	2	2	12	14	46	20(360°)	18
M		6	3	79	82	10(220°)	—	2

The figures are very instructive in view of the respective boiling points of *o*-, *m*-, and *p*-Cresol. Compare B.P. '14, *Fr. Cx.* and *P.G.* requirements, our Vol. I., p. 30.

Unsatisfactory results with the **B.P. test for Phenol in Cresol**. (Cresol 1 Vol. forms with 1 Vol. of Glycerin a clear solution from which the Cresol separates completely on adding 1 Vol. of water.) A better method for its separation and identification is stated to be as follows. Cresol 10 Cc. is shaken with N/10 Potassium Hydroxide 10 Cc., and the mixture allowed to stand or centrifugalised. The upper layer containing most of the Phenate is removed and shaken with Ether to remove uncombined Phenol. This Ethereal layer is rejected and dilute Sulphuric or Hydrochloric Acid is added to the aqueous portion to decompose the Phenate which is shaken out with Ether, separated and allowed to evaporate. This crude separated Phenol is mixed with 10 Cc. Concentrated Hydrochloric Acid and a mixture of Potassium Nitrate and Sodium Nitrite of each 0.2 Gm. in a glass mortar is added and well stirred and allowed to stand from 2 to 5 minutes. A definite crimson or purplish-crimson colour indicates the presence of Carbolic Acid. This can be confirmed by diluting with a little water and pouring into excess of 10% aqueous Ammonia, when, if Phenol be present in very appreciable quantity, a deep emerald-green colour is given.—A. H. Ware, B.P. Conf., 1927, per P.J. i./27,775.

We find working with a 5% admixture of Phenol to Cresol the crimson and the green colors substantiated.

Tests to distinguish Carbolic Acid, Cresols and other Phenols.

TEST I.—Dissolve 1 drop (0.05 Gm.) of the Phenol in 10 Cc. strong Hydrochloric Acid in a mortar and add 0.5 Gm. of a mixture of NaNO₃ (1 part) and NaNO₂ (1 part) and exsiccated Na₂SO₄ (2 parts). Stir well and allow to stand 2 to 5 minutes. Note colour and pour 1 Cc. of the acid mixture into excess of 10% aqueous NH₄OH and note change of colour.

Carbolic Acid gives rich crimson colour in 2 minutes. On pouring mixture into NH₄OH deep emerald green results. If at crimson stage 1 or 2 drops 33% Formaldehyde solution is added and the mixture stirred colour changes to rich purple and if now poured into NH₄OH a deep blue colour occurs. **Ortho-Cresol.** A dichroic solution is given in the acid, green being predominant. If a drop or two of Formaldehyde solution is then added the green changes to blue (purple by transmitted light). If now poured into NH₄OH only olive-green results. **Meta-Cresol, Para-Cresol and Cresol** give no distinctive results and are thus easily distinguished from Carbolic Acid and Ortho-Cresol. The presence of *p*-Cresol also inhibits the reaction with Carbolic Acid or *o*-cresol,

and the test cannot be used for detection of either of these in Cresol, *B.P.* **Beta-Naphthol** and **Alpha-Naphthol** give crimson-purple and violet-purple respectively after standing 3—5 minutes in the acid mixture. Colours destroyed by Ammonia solution. The acid solution withstands heat and subsequent dilution with retention of colour better than with other Phenols. **Thymol**, after stirring and leaving for 5 minutes, gives pronounced green, becoming yellow on pouring into Ammonia solution.

TEST H.—Dissolve 1 drop of the Phenol in 5—10 Cc. strong HCl with a minute crystal (size of pin's head) of NaNO_2 . Slowly heat mixture to nearly boiling: cool or dilute and pour into excess of dilute NH_4OH solution. Note colour changes.

Carbolic Acid, Ortho-Cresol and Meta-Cresol. On pouring the acid solution into NH_4OH and warming, a deep blue colour results. **Para-Cresol** gives no colour in aqueous solution, acidified with Acetic Acid, together with a little NaNO_2 , and a few drops 1 to 2% CuSO_4 solution. A rich wine-red solution is given, turning to pink on dilution with water. **Guaiacol** gives green with NH_4OH . **Resorcinol** gives successively brown, red, purple, violet and blue, and on diluting with water green, and on pouring the acid-mixture into Ammonia solution a dichroic solution with brilliant red fluorescence, wine-purple to transmitted light. **Orcinol, Phloroglucinol** and the **Catechins** give rather poor reds or purples both before and after treatment with Ammonia. **Catechol** gives distinct bluish-green in the acid mixture, and **Pyrogallol** a purplish colour, if heated with a nitrate in the acid mixture.—A. H. Ware, Analyst, 1927, per Y.B.P.'27,186.

We have tried a number of the above reactions and find them satisfactory.

Colour reactions of Phenols with Iron and other reagents.—A. H. Ware.—P.J., ii./28,88.

Assay of Cresols in Lysols.

100 Gm. of Lysol treated with excess 2% Sulphuric Acid, and fatty acids and Cresols extracted with 50 and 20 Cc. of Ether. Ethereal layer is dried over Sodium Sulphate and distilled; Phenols collected between 180 and 230° C.—A. H. Dodd, JI. Soc. Chem. Ind., April 11/24,931.

Cresols in Lysols approximately estimated by steam distillation of 60 to 70 Gm. after acidifying with 30 to 35 Cc. of dilute Sulphuric Acid. The weight of Cresol in the sample is obtained by multiplying the volume of Cresols in the distillate by 1.04 and adding 1/50 of the volume of the aqueous layer. Method gives trustworthy results.—C. J. Jordan and F. Southerton, Analyst, 1921,375. Data also given of a large number of examinations of Castor Oil and Linseed Oil Lysols.—P.J. i./21,479.

Accurate results by distillation can only be assured when the soap is known to be free from volatile fatty acids. It is best to dissolve the sample in hot water in a separator, add a piece of stick Caustic Soda and shake until dissolved. Add excess of brine and separate. Redissolve in hot water, add Caustic Soda and again salt out; repeat again. Acidify the united alkaline liquors and extract with C_6H_6 . Extract this solution with a small quantity of Caustic Soda, acidify and read off in the usual way.—G. F. W. Martin, Y.B.P., '22,142.

Lysol suggested to be added as *synonym* to *Liq. Cresol Sap.* (*B.P.*'14).—P.J. ii./24,508.

Colorimetric estimation of Coal Tar Disinfectants, using a dilution with addition of Sodium Nitrite.—J. Rae, P.J. ii./27,332.

ACIDUM GLYCEROPHOSPHORICUM.

Estimation of Phosphate in Glycerophosphate using Ammonium Molybdate. A reasonable limit of phosphate would be 0.1% (as H_3PO_4). If this limit is present it can be ascertained as follows: 1 Gm. of the glycerophosphate is dissolved in 25 Cc. dilute Nitric Acid, and 5 Cc. of this solution added to 10 Cc. 25% Nitric Acid and 10 Cc. 10% Ammonium Molybdate solution. This should not give a deeper yellow colour than 5 Cc. of a 0.004% solution of Phosphoric Acid, added to 10 Cc. of 25% Nitric Acid and 10 Cc. 10% Ammonium Molybdate Solution.—J. L. Lizius, B.P.Conf., 1921.

The analysis of Glycerophosphate Syrups.—G. Middleton, B.P.Conf., '265 Y.B.P., '26,421.

The alkali and alkaline earth salts of Glycerophosphoric Acid on the English market are for the most part perfectly definite salts and of reasonable purity.

The most noticeable difference between the products of different manufacturers is the considerable variation in the amount of water of crystallisation, especially in the Magnesium and 50% Sodium salts. The majority are not adjusted to a basis of 50% of anhydrous salt. The 50% Potash salt appears to be.—G. J. W. Ferrey, B.P. Conf., '26, Y.B.P., '26, 481.

Calcium Glycerophosphate. Carefully conducted experiments gave a solubility for α salt confirming our 1 in 22. Solubilities for β salt vary—*ibid.*

ACIDUM HYDROCYANICUM.

Volumetric Estimation.—Titrate about 1 Gm. (accurately weighed, kept slightly alkaline with Sodium Hydroxide throughout the test), with N/10 Silver Nitrate Solution, until a permanent Silver Cyanide precipitate is formed. The soluble double salt, $\text{AgCN} \cdot \text{NaCN}$, is intermediate. $\text{AgNO}_3 = 2\text{HCN}$ or 1 Cc. N/10 $\text{AgNO}_3 = 0.0054032$ Gm. HCN.

Borax Solution in excess is added to Hydrocyanic Acid before titration with Silver Nitrate. Suitable for Cherry Laurel Water.—P.J. ii./05, 910.

The official method gives practically the same percentage as the old soluble double salt $\text{AgNa}(\text{CN})_2$ method. The presence of chloride makes no appreciable difference. Excess of alkali causes only a slight error.—D. B. Dott, P.J. i./16, 368.

Determination of Hydrocyanic Acid.—C. E. Corfield and C. J. Eastland, B.P. Conf., 1921.

Volatility of Hydrocyanic Acid at ordinary temperature in an open vessel may be considerable.—*ibid.*

R. Leitch Morris has reviewed the various known methods. The B.P. process apparently uses too little Potassium Iodide. Three or four times the amount gives better result.—B.P. Conf., 1920.

Quantitative Estimation of Hydrocyanic Acid in the blood and tissues of animals post mortem. The method is colorimetric and depends on reaction between Potassium Cyanide and Picric Acid. [Liebig's Annalen, CX. p. 289 (1859)]. A Color Scale for comparison is made by mixing equal volumes of recently titrated 1/1000 HCN and Picrate mixture (equal volumes of 0.5% Picric Acid and 5% Sodium Carbonate). This stock solution (T 500) is further diluted (T 1, 2, etc.). The estimation is made by matching the color of the given fluid or of its distillate into Picrate Mixture with that of the color scale.—A. D. Waller, Phys. Proceedings, June 18, 1910.

Detection of Traces of Hydrocyanic Acid.

A comparison has been made of the delicacy of the Prussian blue as compared with the picrate test for hydrogen cyanide, from which it appears that the former is of at least equal delicacy to the latter.

By evaporating the Alkaline Cyanide Solution to almost complete dryness, adding 2 per cent. Ferrous Sulphate, leaving *in the cold* for ten minutes and acidification, evidence of the presence of 0.000002 Gm. of HCN may be obtained. The Ferro-Cyanide reaction may be used for the detection of Hydrogen Cyanide in the blood and brain of poisoned animals with equal efficiency to the Picrate method as applied to the same purpose by Waller.—G. D. Lander and A. E. Walden. Chem. News, May 19/11, p. 240.

See also Water Analysis chapter.

Delicate Test for Hydrocyanic Acid.—A few drops of phenolphthalin solution made alkaline with Sodium Hydroxide added to liquid to be tested. If red colour be produced on adding Cupric Sulphate Solution 1 in 2,000 (due to oxidation into phenolphthalein) Hydrocyanic Acid is proved to be present. Phenolphthalin is made by reducing phenolphthalein with Zinc in alkaline solution.—P.J. i./05, 721.

Place 1 drop of 1:5 Ammonia Dilution on a microscopic slide and invert over tube containing the solution to be tested, together with a few drops of Sulphuric Acid. After a few minutes remove slide and place under microscope: on the addition of 1 drop of Alloxan solution (made by boiling 0.1 Gm. Uric Acid with 0.2 Cc. Nitric Acid and 0.2 Cc. water and diluting 5 Cc.) crystals of Oxaluramide begin to form in a few minutes if the test solution contains a Cyanide. Substitution of Pyridine for Ammonia renders test far more delicate so that a few drops of a solution containing 0.01 Gm. HCN per litre gives positive results.—per Y.B.P., '27, 168.

As a **Bactericide (fumigant in ship disinfection)** Hydrocyanic Acid is too weak to affect pathogenic germs. It has no measurable Carbolic

Acid Co-efficient. *Less than 0.02.*—W. C. Reynolds, L. ii./22,834. Its danger. P.J. i./23,300. It destroys rats, fleas, etc. It has no ill effects on dry grain, but moist food, *e.g.*, butter, milk, etc., is liable, to absorb the gas.

To destroy bugs Hydrocyanic Acid is much used in S. Africa. Stringent regulations control its use and the licensing of disinfectors employed.—O. Porter, L. ii./21,583.

While a concentration of 2 Gm. of HCN per Cc. of air will kill an animal in a few minutes, animals given a previous dose of Glucose, by injection or by mouth, can breathe this atmosphere for more than an hour without ill-effects.—L. ii./26,94.

ACIDUM HYPOCHLOROSUM.

Eusol.

Preservation.—Keep in stoppered bottles away from the action of light. The preparation maintains its strength for 3 weeks in cold weather. In hot weather it should not be kept more than 1 week. It is preferably made fresh each day for use on the day following.

Loss in Strength.—We have kept bottles of Eusol under observation for four months, titrating them at frequent intervals, and have found the loss in strength to be most marked.

Dakin's solution, however, keeps much better.

Assay.—Place 25 Gm. of the solution in a flask, add about 1 Gm. of Potassium Iodide and 5 Cc. of Acetic Acid and titrate with N/10 Sodium Thiosulphate solution, using starch paste as indicator. Each Cc. of the Thiosulphate solution employed shows 0.00262 Gm. of HClO (or 0.00354 Gm. available chlorine).

As an alternative process titrate 25 Gm. with addition of a little Sodium Bicarbonate with N/10 As_2O_3 solution (4.95 Gm. per litre), adding this solution from a burette until a drop removed on a stirring rod mixed with a drop of Potassium Iodide-Starch paste on a white tile no longer produces a blue color. Each Cc. of the As_2O_3 solution used shows 0.00262 Gm. HClO and 1 Cc. of Standard Eusol = 1 Cc. of N/10 Arsenious Oxide.

We found it of importance to liberate the Chlorine first of all in Acid (HCl) solution in doing this titration, *then* add Sodium Bicarbonate and titrate, otherwise the reading will be far too low.

Solutions of this nature may be slightly pink in color if Manganese is present in the bleaching powder.

Bactericidal Power—Hypochlorous Acid is a more potent bactericide than its salts. The acid is stated to be the most powerful antiseptic known. It was found to be as active against Anthrax spores as against non-spore-bearing organisms (2 minutes' contact).

Dakin's (Weaker) Hypochlorite Solution.

Strength—Dakin's (weaker) solution, and his stronger solution on dilution are approximately 1/5 the strength of Liquor Sodæ Chlorinatae, and there is a considerable excess of sodium carbonate employed. This is neutralised with Boric Acid as described in Vol. I., p. 49.

Some confusion arises in the expression of the strength of preparations of this kind. This weaker preparation contains 0.5 to 0.6% of Sodium Hypochlorite, which is equivalent to 0.48 to 0.57% available chlorine or 0.35 to 0.42% Hypochlorous Acid.

The stronger Dakin Solution is approximately 7 times these strengths. **Bactericidal Power.**—The antiseptic power of Sodium Hypochlorite using *Staphylococcus Aureus* with 2 hours' contact (1) in water, it is stated, lies between 1:500,000 and 1:1,000,000, while in the presence of Blood Serum the necessary concentration is between 1:1,500 and 1:2,000.

By "Hypochlorite" is clearly meant the 0.5% NaClO contained—in other words, to kill the organism in water in 2 hours between a 1 in 2,500 and a 1 in 5,000 dilution of the solution is requisite, whilst in the presence of serum between a 1 in 7.5 and a 1 in 10 dilution is necessary. The solution is hence not extraordinarily powerful.

It appears to us that the 2 hours contact is an extraordinarily long time to permit the antiseptic to act for purposes of comparison with other potent antiseptics, and may give rather a distorted interpretation.

It is stated that Iodine between 1 : 100,000 and 1 : 1,000,000 killed Staphylococci in water in 2 hours—the idea being to prove “Hypochlorite” more active—but we found in experimenting in 1914 that 1 : 50,000 Iodine would kill the generally used Test Organism *B. Coli* in $2\frac{1}{2}$ minutes, and considering that 1 : 75,000 of chlorine, we found (1914), also kills this organism in $2\frac{1}{2}$ minutes, we fail to see the object in using the 2 hours time limit.

Chloramine-‘T.’

The theory appertaining to the use of this substance as an antiseptic is that Hypochlorous Acid acting on protein and allied bodies containing the =NH group effects a substitution of the H atom by Cl with formation of Chloramines.



These Chloramines in themselves are all potent antiseptics and bodies of this type are formed in wounds when treated with Hypochlorite antiseptics. A soluble Chloramine compound was looked for, which led to the selection of *p*-Toluene-Sodium-Sulphonechloramide and the Benzene analogue, both of which can be used in higher concentration than the Hypochlorites. The simplest Chloramine NH_2Cl is probably formed during treatment of sewage by Hypochlorite.—H. D. Dakin, B.M.J. ii./15,318,810.

Bactericidal Power.—Chloramine - ‘T.’ 1 : 1,000,000 in water with 2 hours’ contact kills staphylococci and in the presence of serum the strength for this and the Benzene analogue required is between 1 : 1500 and 1 : 2500. The Benzene analogue is only half as active in water as the ‘T’ body—1 in 500,000 being required. In concentration below 1 in 10,000,000 the Toluene body kills *B. Perfringens* in water in 2 hours.—B.M.J. ii./15,262.

Molecule for molecule it is thought to be 4 times as active as Sodium Hypochlorite. Almost all the aromatic bodies containing the NCl group are active bactericides. More than one NCl group in the molecule does not increase power.—B.M.J. i./16,388.

Germicidal power of chlorine antiseptics (Chloramine-‘T,’ etc.) as compared with Acriflavine, etc. The former are far more potent (in the presence of serum). The technique employed by Browning gave misleading data.—H. Dakin and G. K. Dunham, B.M.J. ii./17,641.

“Activin.”—Under this name Chloramine-‘T’ suggested as a general bleaching agent, and suitable for laundries—more effective and less destructive to fabrics than Sodium Perborate, although less active than the Hypochlorites.—Na., 114, '24,625.

Chloramine-‘T’ has been suggested to replace the more expensive Iodine solution in analytical processes.—J.C.S., A. ii./25,66.

ACIDUM LACTICUM (B.P. '14).

P.G. VI. requires (with Sp. Gr. 1.206 to 1.216) total acid 90%, of which about 72% is free acid, reckoned as Lactic Acid. Assay process: 5 Gm. of Lactic Acid is diluted with water to 100 Cc. 40 Cc. of this mixture is neutralised with N/1 KOH, in presence of Phenolphthalein, using approx. 16 Cc. of test solution (=72% of Lactic Acid). Further 5 Cc. of N/1 KOH is added and the mixture warmed 5 minutes on the water-bath until the pink colour of Phenolphthalein has disappeared. Then 2 Cc. of N/1 HCl are added with further 2 minutes warming. The excess acid is back titrated. The total N/1 KOH used less the total N/1 HCl must be approx. 20 Cc., i.e., approx. 90% total acid.

(B.P.'14 contains not less than 75% Lactic Acid and not less than 10% Lactide.)

Lead should not exceed 10 parts per million.

Detection of Lactic Acid.

A bright red coloration is obtained when 0.2 Cc. of solution, containing less than 0.2% lactic acid, is heated for two minutes at 100° with 2 Cc. conc. H_2SO_4 , cooled and treated with two drops of 5% alcoholic guaiacol solution.

This reaction is not given by formic, acetic, malic, benzoic or salicylic acids. Citric acid gives yellow color, tartaric acid a slight red color, and tannin a blackish-violet.—J.C.S.A. ii./21,356.

ACIDI LACTICI BACILLI.

Lactic Acid Bacilli Preparations.

To arrest growth of putrefactive (alkaline) organisms in the intestines and hence stimulate intestinal digestion and diminish toxic absorption from the bowel Prof. Elie Metchnikoff proposed the acclimatisation of the (harmless) Lactic Acid Bacillus. The newly-born infant has sterile intestines and on partaking of the first drop of mother's or cow's milk these commence to be infected. Evils result from putrified food, some of the recipients dying from the effects; others if their resistance be sufficient, saving their lives after experiencing a severe attack of cholera. Acidity makes its appearance in connection with the custom prevailing from early times of preserving food with vinegar—the product of bacteria to 'ward off putrefaction.' Substances themselves producing a preservative acid—*e.g.*, milk,—can be made into others—*e.g.*, cheese—which can be kept for longer or shorter periods of time. Experimental consumption of large quantities of Lactic Bacilli showed that intestinal putrefaction was diminished.

It was found that with a normal diet the Bacillus appeared in the stools in three to four days after it had been consumed regularly with the food; that it took eight days to become properly acclimatised in the intestine, and that when this had taken place it would continue to live and thrive for twelve more days without another dose being swallowed, afterwards gradually disappearing. Regular administration caused increase in weight and bulk of fæces (*cf. work under B. Acidophilus postea*).

Lactic Acid, as such, has been employed for years past in dyspepsia, enteritis, etc., and locally in tuberculous ulceration of the larynx.

The conclusion was that as organisms of putrefaction only increase with difficulty in neutral or acid media, the most feasible procedure would be to introduce a Lactic Acid organism (growing in a sugar medium) into the human being to arrest the proliferation of harmful bacteria. The bacillus known as the **Bulgarian Bacillus** (*B. Caucasicum*), isolated by Cohendy and independently by Massol from 'Yoghourth' a form of soured milk, was deemed most suitable, as it is the best acid producer. The acid it produces is the optically inactive variety. It is a hardy organism resisting the stomach juices and its own acidity to a marked degree.

According to Hewlett it occurs apparently in various forms. In natural soured milks *B. Bulgaricus* and *B. Massol* from Bulgarian Yohourt and Maya, *B. Mazun* from Armenian mazun, *B. Lactis Acidi* (Leishman), etc., are probably varieties of only one species.

Buttermilk in many countries, **Kephir** or **Koumiss**, *vide Vol. I. p. 589*, the Egyptian 'Leben Raib,' 'Prostokwoeha,' and 'Varentez,' of Russia, Yoghourth (Yohourt) of the Balkans, and many others, were forerunners of the curdled milk treatment, which attracted so much attention. It is believed that the Bulgarian peasant consumes as much as 10 Gm. of Lactic Acid daily in his diet of Yohourth.

In Sardinia, the people prepare and make a continuous diet (for lack of anything better) of Gioddu Mezzoraddu, or Miciaratu, which are the products of fermentation due to *Saccharomyces Sardons* and to *Bacillus Sardons* and *Mazun*, and which resemble in composition the Lebenraib of Egypt, the Prostokwoeha and Varenetz of the Russians, the Kephir of the Caucasians, the Koumiss of the Tartars, and the Mazun of the Armenians. At Milan the grape ferment is in demand, at Turin Blastoinvertin (*Saccharomyces invertens*) in Lombardy Kephir, and at Piedmont the true Yohourt.

In Greece Yohourt is much in use both as a food and for treatment. It is prepared there by adding a little lemon-juice to fresh milk, which is kept warm for eight hours, forming a curd. From the curd a tablespoonful is mixed with boiled milk, and this procedure is repeated several times, with fresh milk on each occasion, until a Yohourt of suitable consistency is obtained. Small spoonfuls of this latter product are added to wooden or earthenware pans containing milk which has been boiled and is still slightly warm. This forms the commercial Yohourt, which curdles in four hours at 35° C. It has at first a sweetish taste, becoming extremely acid after twelve hours. In order to keep it, and this one may do for as long as from five to eight days, it is poured into little bags of cotton from which the whey filters, the product thereby becoming thicker and of better-keeping qualities. Yohourt prepared from sheep's milk is highly esteemed as a milk-food by the Greeks.

These sour milks, as a rule, contain yeasts in small proportions, and *ergo* alcohol—the same remark applies to the artificially soured milks.

The presence of yeast may be a useful therapeutic aid.

The **Bulgarian Bacillus** will produce as much as 2·5 Gm. of Lactic Acid per 100 Cc. of milk.

Succinic, acetic and formic acids are also formed by it in small quantity. This bacillus has no action on albuminoids (casein, etc.) nor fats, nor does it produce alcohol or acetone. It **does not attack saccharose (cane sugar)** or maltose; it is therefore useless to add cane sugar in the hope of increasing Lactic Acid yield.

Gunther's Bacillus is found in abundance in all spontaneously coagulated milk and is an important Lactic Acid producer. Its presence in curdled milk is thought to improve the flavour and to modify the condition of the curd. It produces pure dextrorotatory Lactic Acid (no other acid) from grape and milk sugar.

Hüppe's Bacillus is another Lactic Acid organism.

It is almost always present in milk which has soured spontaneously. This organism, sometimes called specifically the *B. Acidi Lactici*, differs from *B. Guntheri*, by its comparative ease of cultivation upon ordinary media.

The characters of the chief Lactic Acid organisms may be tabulated:—

ORGANISM AND	APPEARANCE.	PROPERTIES.
<i>Bacterium Caucasicum</i> (Kern); <i>Syn.</i> Massol's Bacillus, Bouchard's Bacillus, Bulgarian Bacillus.	Large square-shaped, 5 to 6 $\mu \times 1 \mu$ showing vacuoli, slightly motile. + Gram staining.	Takes time to establish but ultimately is the omnipresent bacterium in milk. A strong lactic acid producer.
Hüppe's Bacillus: <i>Syn.</i> <i>B. Acidi Lactici</i> . <i>Streptococcus Lebenis</i> may be closely allied.	Coccoid shape 0·4 to 0·6 $\mu \times 0\cdot6$ to 2 μ ; in pairs, rarely chains, non-motile. + Gram staining (opinions differ.)	Causes bitterness, breaks up fat and proteolytic substances.
<i>Bacterium Guntheri</i> , <i>Syn.</i> <i>B. Acidi Paralactici</i> (Kozai).	Short rods, 1 $\mu \times 0\cdot5$ to 0·6 μ , with pointed ends, in pairs or short chains non-motile. —Gram staining.	Gives a smooth curd; appears to be ousted to some extent in curdling by <i>B. Caucasicum</i> .

Yohourt. Preparation—Raise the milk to boiling point. Remove from the heat and cool enough for a skin to form on top. While still too hot to be held conveniently inoculate by allowing some previous Yohourt—thinned with sterile water, if necessary—to slip down the edge of the container all round the rim. Cover, and, without shaking, place in a closely fitting hay-box until the next day. Do not allow to cool before placing in hay-box.—J. Graham Willmore.

Methods of Examination of Lactic Acid Bacilli Preparations.

Loopfuls of the milk, treated with a crushed Lactic Acid Bacillus tablet (*vide* Vol. I.), are to be examined after ten and twenty-four hours' cultivation.

Stain by 'Gram,' using 1% neutral red as counterstain. The Gram-staining organisms are deep violet, the rest of the field reddish pink. A copious growth of *B. Caucasicum* is essential, with exclusion of other bacteria.

Curd formation should also be satisfactory. The property of producing lactic acid is common to a vast number of organisms.

Lactic acid content depends on the lactose content, the average of the latter being 4 per cent. The decomposition of lactose in milk into lactic acid is a complex matter. Nature will not allow a theoretical yield, as the bacilli kill themselves by the acid they produce—the maximum acid formation being reached in about thirty-six hours. The *activity of the culture* is more important than the quantity of acid.

The maximum amount of acid is about 0·8% or more if longer time is allowed.

Milk, it should be noted, is amphoteric in reaction on account of its content of alkali phosphate. 20 Cc. is a convenient quantity to titrate, using N/10 Soda and Phenolphthalein.

For details of CASEIN and PHOSPHATE RENDERED SOLUBLE, see a paper by the author, 'Lactic Acid Organisms.'

References.

Metchnikoff found *B. putrificus*, *B. Sporogenes*, and *B. Welchii* (*B. Aerogenes Capsulatus*) inhabitants of the large intestine.—B.M.J. ii./09,1024.

The useful role of the lactic acid consists in preventing changes in the proteins beyond a certain point. Once established, the lactic bacilli counteract the action of such bacteria as *B. Coli*, which splits up proteins beyond the desired limit, with production of toxins, etc., and diminishes the amount of nutrition supplied to the blood.—L. ii./08,958.

Symbiosis in nature plays a large part in the destruction of infective organisms—by crowding out. The fact that the lower animals do not become infected through the digestive tract with typhoid and cholera is ascribed by Metchnikoff to this symbiosis.—Hewlett.—L. i./09,743.

B. Caucasicum, according to the late G. Herschell, resists gastric digestion, reaches the intestines alive and establishes itself as a part of the intestinal flora with a limited life of a few weeks, becoming a facultative anærobe living on the culture medium provided by the food of the individual.

Metchnikoff's opinion was "that if it be true that our precocious and unhappy old age is due to poisoning of the tissues (the greater part of the poison coming from the large intestine, inhabited by numberless microbes), it is clear that agents which arrest intestinal putrefaction must at the same time postpone and ameliorate old age."

In a later paper Metchnikoff stated that senility is attributable largely to poisons, aromatic bodies, Indols and Phenols of the intestinal flora. Diet should be arranged to reduce these bodies. Lactic Acid Bacilli are necessary to overcome toxin-forming microbes.

Amongst the highly beneficent organisms in the intestinal flora, in the French view, are the acetogenic organisms and of these in particular the *B. bifidus* of Tissier (Anaerobe and Gram +).

Indol is produced by Coliforms and only to a small extent by the putrefactive anaerobes (*B. putrificus*, *B. Perfringens*, *B. Sporogenes*, etc.). Ledingham remarks it is surprising that Metchnikoff should have drawn so much attention to the anaerobes as the chief factors in intestinal putrefaction while at the same time devoting so much energy to the investigation of the toxic action of Indol—a product chiefly of coliforms. The conclusions are contrary to the researches of the Metchnikoff school.—L. i./13,1153.

B. Acidophilus.

In Gram-stained smears from human fæces and from milk and whey-broth cultures, *B. acidophilus* appears as a rather long, stout, Gram-positive rod, characteristically curled towards the ends. Great variation occurs in length. Some varieties occur as short Gram-positive bacilli, with a tendency to chain-formation, especially on isolation from rats' or dogs' fæces. In cultures on whey-agar two types of colony of *B. acidophilus*, designated "X" and "Y," are frequently seen side by side. The former have a decidedly fuzzy appearance and are indistinguishable from *B. Bulgaricus*, while the latter is small round or spindle-shaped, only partly fringed and at times almost perfectly smooth. The "X" colonies can be differentiated from *B. Bulgaricus* by the fact that *B. acidophilus* produces acid in 1% maltose broth after incubation at 37° C. for 48 hours, while *B. Bulgaricus* does not. The implantation of *B. acidophilus* in the intestine is possible. *It was not found possible to implant B. Bulgaricus in the intestine by giving milk infected in the usual way. This may be due to the fact that unlike B. acidophilus, it is not a normal inhabitant of the human intestine.*—Ralph P. Smith, B.M.J. ii./24,948.

A STUDY OF *B. ACIDOPHILUS* IN HUMAN FÆCES.—The term "*B. acidophilus*" may cover a considerable group of organisms and numerous strains may exist even in one sample of food.—J. Cruickshank and D. W. Berry, B.M.J. ii./24,944.

Of 8 commercial 'Acidophilus' products only 5 stated on the label the number of viable organisms and of the 5 only 3 fulfilled their claims.—Jl.A.M.A., ii./28,1192.

ACIDUM PHOSPHORICUM.

B.P.'14 Assay Method.—A process is given for titrating with N/1 Sodium Hydrate in presence of Sodium Chloride. Lead limit 10 per million. Arsenic 5 per million.

U.S.X. requires 85 to 88% pure.

The best method for the complete titration of P_2O_5 , NaH_2PO_4 and Na_2HPO_4 is the use of Phenolphthalein at the temperatures 55–70° C., after $CaCl_2$ has been added to the phosphate solution. The proportion of phosphate to $CaCl_2$ should be 1 in 2 to 1 in 5.—Per Y.B.P., '26,305.

Metaphosphoric Acid $HPO_3=80.035$ is equivalent to *Glacial Phosphoric Acid*, and is employed as an Albumin Test. (*vide Urine*).

Pyrophosphoric acid $H_4P_2O_7=178.086$ is an opaque white crystalline solid and is formed as an intermediate compound in the hydration of metaphosphoric acid. The hydration does not take place according to any simple scheme, and a method of estimating meta acid in a solution of all three varieties by means of barium chloride is described. From the depression of the freezing point of aqueous solutions of various varieties of pyro and meta acids, it appears that when these acids are prepared by dehydration of ortho-phosphoric acid there occurs association of the molecules, but when prepared by decomposition of the lead salts by hydrogen sulphide simple molecules result.—Myers & Hold, *Manch. Phil. Soc.*, per Na., March, 11,66.

ACIDUM PICRICUM.

If confined, Picric Acid explodes somewhat more readily than Ammonium Picrate, but with slightly less vigour, when heated in a test tube. The Acid does not explode on striking with a hammer on an iron plate. As a high explosive it is used in shells, *e.g.*, as **Lyddite**, **Melinite**, etc. It is safe, *i.e.*, it is sufficiently insensitive to shock to prevent it being exploded when struck by projectiles or fired from a gun. T.N.T. is less sensitive to shock than Picric Acid, and is unaffected by water and metals. A solution precipitates most alkaloids. *Cf. Scheme for Recognition of Organic Chemicals.*

Eugene Turpin in 1885 discovered that, provided the initial ignition is of sufficient violence, pure Picric Acid is one of the most powerful explosives. He also showed that the substance could be poured in a molten condition or be pressed in to shells or grenades. Turpin's Shell which is essentially the same as modern high explosive shell, comprises the shell body filled with the acid the point of the shell containing priming which is exploded by means of a percussion detonator. As the substance melts somewhat high, and this is inconvenient for working, various additions have been made to lower the melting point, *e.g.* Nitro-Naphthalene, Camphor, T.N.T., etc. Various names were adopted, *e.g.*, Melinite, Lyddite, Schimose (Japanese) etc.

Many accidents have occurred in its manufacture and filling—generally attributed to contact with metal oxides, chalk, brickwork, etc., and hence the formation of salts, the intermediate formation of these picrates resulting in the detonation of the acid. Picric Acid has been largely displaced by T.N.T.—From 'High Explosives,' by E. de W. S. Colver, 1918.

Quantitative Estimation.—Nitron (*cf. Acid. Nitric. Vol. I. p. 60*) precipitates picric acid and can be used for the purpose.

Determination of Picric Acid and Ammonium Picrate with Titanous Chloride.—A. A. Boon and J. Ogilvie, *P.J. ii./16,213*.

A mixture of Ammonium Picrate and Potassium Nitrate is frequently used as a priming for shells filled with Picric Acid, particularly in Lyddite Shell.—'High Explosives,' by E. de W. S. Colver, 1918.

ACIDUM SALICYLICUM.

Use as Preservative (*Not now allowed*) See Food Preservative Regns.

It has the disadvantage of sometimes giving the odour of phenol. Its use, where otherwise rapid decomposition would occur, has been upheld by some in the past, *e.g.*, 1 grain per pint or 1 grain per lb.

Detection.—Concentrate liquid (distil off any alcohol) in presence of Alkali and Sodium Chloride, acidify and shake out with Chloroform, evaporate and add Ferric Chloride Solution—violet colour. *See also Scheme for Recognition of Organic Chemicals, Acidum Benzoicum, Food Preservatives, and Antiseptic Power Chapter.*

Self's Vanadate Test for Salicylic Acid.

Mix equal parts by volume of 40% Formaldehyde and Conc. Sulphuric Acid and cool the mixture thoroughly. Moisten the substance to be tested in a dish with the mixture, add a little Ammonium Vanadate and stir well. If Salicylic Acid is present a Prussian blue colour appears immediately changing rapidly to greenish blue, and finally green. For about 1 mgr. of Salicylic Acid use two drops of the liquid and 2 to 3 mgr. of Ammonium Vanadate. The only other substance giving the colour is Salicylic Aldehyde.—P.J. i./15,521

3 : 5 Dibromosalicylic Acid is considerably more active than Salicylic Acid as a bactericide.—Y.B.P., '27,227.

Adsorption through the Skin.

Salicylic Acid can be transported through the epidermis into the connective tissues and thence into the blood stream. The colloids of the connective tissues retain the drug by adsorption and from these surfaces it is liberated gradually, passes into the blood and is mainly excreted by the kidney. The excreted portion may be estimated colorimetrically in mg. per 100 Cc. urine, and if the quantity of urine voided in the 24 hours is known the total urinary excretion of Salicylic Acid may be calculated. Adsorption may take place from Soft Paraffin, Alcohol and Water, but the first is probably best.—H. Leslie-Roberts, Brit. Jl. Dermat. & Syph., Aug., '28,325; per Jl.A.M.A., ii./28, 1409.

Sodium Salicylate.—Solutions with Sodium Bicarbonate become dark due to oxidation. A small quantity of Sodium Sulphite, bisulphite or hyposulphite prevents discoloration.—H. G. Greenish & A. E. Beesley, P.J. i./15,210.

ACIDUM ACETYL-SALICYLICUM.

The *melting point* of pure Aspirin considered as the temperature of formation of the first liquid globule, is 133.5° when the substance in a m.pt. tube is inserted in the bath at 130°, the temperature of which rises exactly 3° per minute.—M. E. Putnam, Ind. Eng. Chem., '24,16,778, per J.C.S., A.i./24,1070.

Test for Aspirin and its Derivatives.—(V. Arreguine and E. D. Garcia, Ann. Chim. Analyt., No. 2, 1920, abst. C.D. Oct. 2/20,1364), depending on the formation of *B*-methyl-umbelliferone by interaction with Resorcin.

We have employed a solution of 0.1 Gm. Aspirin in 100 Cc. dilute Alcohol, using small quantities of this for the test.

Mix 0.1 to 0.2 Gm. Resorcin with 2 or 3 Cc. of a solution of aceto-acetic ester in concentrated hydrochloric acid (1 Cc. in 10 Cc.) in a test tube. 1 Cc. of the above Aspirin solution is added (equiv. to 0.001 Gm.) and the mixture boiled for a few minutes and allowed to cool. A small amount of water is added and the whole made alkaline with ammonia. A blue fluorescence is produced.

With 0.1 Cc. of the Aspirin solution (equivalent to 0.00001 Gm. of Aspirin), the fluorescence is also obtained.

On repeating the test *without* Aspirin we found the fluorescence also appears to a slight extent. It would be necessary to do a control for comparison.

Tests for purity of Acetyl-Salicylic Acid and its Salts.

A solution yields a buff-coloured precipitate with Ferric Chloride until hydrolysed by the addition of a little Hydrochloric Acid, which yields the typical violet colour of Salicylate (developing particularly on warming).

The Ferric Chloride Test for *free Salicylic Acid in Acetyl-Salicylic-Acid* is inefficient to prevent adulteration, etc., in that the addition of Borax, Sodium Phosphate, Tartaric Acid, Citric Acid and other Oxy-acids will readily prevent or mask the colour ordinarily produced with Ferric Chloride.

Tartaric Acid added to Aspirin Tablets would mask the Ferric Chloride test of the B.P.'14 if Salicylic Acid were present. 1% of Citric Acid will mask the presence of 0.2% of free Salicylic Acid.—A. Nutter Smith.—C.D., Nov. 27, 1920, p. 1630 (from 'The Analyst.')

The test is, however, very useful for observing hydrolysed acid. We have used it in the following investigation. Modifications have been employed to determine the purity of the compound.

Hydrolysis of Acetyl-Salicylic Acid and its Salts in Dilute Acid and in Water.

The following table, according to our experiments in 1911 and 1925, shows the results for the hydrolysis of Acetyl-Salicylic Acid and its Calcium, Magnesium and Sodium salts in water and in Physiological Acid (0.2% HCl) **at 38°C.**

The solutions used were 1 in 500, and the amount of Salicylic Acid formed was determined by diluting 25 Cc., or less, of the solution to 50 Cc., adding 1 Cc. of 1% Ferric Chloride solution and comparing in Nessler cylinders with the colour given by a standard Sodium Salicylate solution.

When the solution to be tested contained Hydrochloric Acid, an equivalent amount of N/4 Caustic Soda solution was added before the Ferric Chloride, to ensure that the color should not be interfered with by the acid.

COMPOUND.	SOLUTION.	PERCENTAGE HYDROLYSIS.						
		Immed. on dissolv- ing.	After 1	2	3	4	5	24 hours.
Acid Acetyl-Salicylic.	In water ..	Nil	0.5	1.3	2.0	2.9	4.0	20%
	In 0.2% HCl.	Nil	1.3	2.4	3.9	4.7	7.6	38%
Magisal.	In water ..	2.2	3.3	5.5	7.8	9.1	12.5	33%
	In 0.2% HCl.	2.2	3.3	5	5.5	7	8	28%
Tylcalsin.	In water ..	1.6	3.2	6.3	9.5	10	14	38%
	In 0.2% HCl.	1.6	3.2	4.6	5.4	7	8	35%
Tylnatrin.	In water ..	1.5	2.9	6	7.3	8.8	11.7	30%
	In 0.2% HCl.	1.5	2.9	4.4	5.3	6.5	7.3	30%

It is seen from these results that the amounts of Acetosalicic Acid and its salts hydrolised after three hours' treatment with Physiological Acid are slight, and show no great difference. Hence, the alkaline salts may be quite as useful in physiological action as the acid itself, and by reason of their greater solubility—in particular the Calcium salt—should possess distinct advantage for prompt action.

The 24-hour results are given in the tables as matters of chemical interest, rather than as being of physiological importance.

The **conclusion** is that in taking a dose of Aspirin, or its salts, **the amount split up while passing through the stomach does not exceed 5% of the amount taken.**

The following supports our views:—

The rate of hydrolysis is minimum in neutral solution, but markedly increases in presence of acid or alkali. At P_H 5.5, 34% is hydrolised in 18 hours, and at P_H 8, 45%. It is suggested that Aspirin ought to be fairly stable in the buffer mixtures encountered in the alimentary canal, and in support of this it is stated that, after administration, varying quantities of 5.3% to 41% may be recovered from the urine.—J.C.S., A. i./23,879.

Tunncliffe demonstrated presence of Salicylic Acid in the gastric juice (syphoned off) $\frac{1}{2}$ hour after taking 1 Gm. of the Acetylated Acid. Pancreatic juice also splits up the acid rapidly.

Physiological Action.

R. Stockman, B.M.J. i./13,598, says that in presence of alkalis, *i.e.*, in the duodenum, the ACID is split up forming Sodium and other Salicylates. It is doubtful, however, whether the whole of it is thus changed, as it is a much more powerful analgesic than Sodium Salicylate, and this can only be accounted for by assuming that a part of it is absorbed as such unchanged. Patients agree that even in non-rheumatic affections it lessens pain. This is true only to a very slight extent in the case of Salicin or Salicylic Acid.

We dealt further with this matter in previous editions. The view generally held is that the **bulk of the acid is absorbed in the intestines after hydrolysis.**

Hydrolysis of Magisal, Tylnatrin and Tylcalsin in Solution with Potassium Bromide and Sodium Chloride.

It follows as a sequel to the data provided, that the splitting up of the various Aspirinates in dilute solution and the consequent amounts of Acetic Acid formed are small. The matter came under consideration in our laboratories recently on the suggestion of W. E. Picton Phillips, in the case of solutions of the compounds in conjunction with a therapeutic dose of Bromide to be employed as an injection *per rectum* after operation.

The data obtained were as follows:—

SALT.	MAGISAL.	TYLCALSIN.	TYLNATRIN.
Composition of solution.	Magisal 20 grs. Pot. Brom. 1 dr. 1% NaCl—1 pint.	Tylcalsin 15 grs. Pot. Brom. 1 dr. 1% NaCl—1 pint.	Tylnatrin 15 grs. Pot. Brom. 1 dr. 1% NaCl—1 pint.
Amount hydrolysed directly after making	1·8%	0·7%	0·2%
After 18 hours at room temperature.	6%	5·4%	5%

In other words, in any of the three cases, the amount of actual Acetic Acid formed in 18 hours is only in the region of 1 in 30,000. After three days, the amount was in the region of 33%, more or less, in each case, *i.e.*, roughly 1 in 5,000 Acetic Acid—the other products being a Magnesium, Calcium, or Sodium salt.

A combined enema made on these lines would therefore be perfectly safe, and in practice we were informed that in numerous cases the injection with Magisal gave the patient a comfortable drowsiness for some hours, with little or no post-anæsthetic vomiting.

Determination of Free Salicylic Acid in Aspirin.

Shaking the crystals with water as mentioned in B.P. '14 method is not satisfactory.

Dissolve Salicylic Acid 1 Gm. in Alcohol 60 Cc. and adjust to 100 Cc. with water. 10 Cc. of this solution may then be diluted to 1,000 Cc. for the standard, making 1 Cc. = 0·0001 Gm. Acid.

Dissolve 0·6 Gm. of the Aspirin to be tested in 9 Cc. of Alcohol (S.V.M.), dilute with water to 30 Cc. and mix well. Take two exactly similar Nessler glasses. Into one pour 60 Cc. of the solution, into the other the remaining 30 Cc., together with 3 Cc. of alcohol, and adjust to the volume of the first. This gives a difference of 0·2 Gm. of Aspirin in similar mixtures of alcohol and water. One Cc. of a 1% solution of Iron Alum is added to each, mixed, and the colour matched by adding the salicylic acid solution.—A. J. Jones.

We have tried this test. In the case in point 5·5 Cc. of Standard solution were needed.

Therefore the 0·2 Gm. of Aspirin was matched by 0·00055 Gm. free acid—*i.e.*, the sample contained 0·275% free Salicylic Acid.

A sample of Tablets contained 0·31%.—W. H. M., 1920.

Limit of Free Salicylic Acid.—0·15% has been suggested as reasonable limit and 0·2% in tablet form. This seems to us rather stringent.

Determination of Free Acetic Acid. A. Nutter-Smith (B.P. Conf., 1920) described a process by which the sample (1 Gm.) previously finely powdered is spread on muslin and the Acetic Acid evolved is aspirated into 50 or 100 Cc. of Distilled Water for $\frac{1}{2}$ or 1 hour. The liquid is then titrated with N/500 Caustic Soda. Each Cc. of this represents 0·00012 Gm. Acetic Acid.

The B.P. '14 Test, it is said, is not sensitive unless about 0·04% free Salicylic Acid is present.

Potassium Citrate with Aspirin. In Vol. I., p. 75, we deal with the increased solubility of Aspirin when admixed with Potassium Citrate—the practical upshot being that Aspirin can be rendered soluble 1 in 20 when nearly twice the amount of Potassium Citrate is present.

T. Wilson, P.J. i./29,196; C.D. i./29,286, writes concerning a mixture containing Aspirin 3 drachms, Potassium Citrate 6 drachms, and Water to 6 ounces, which involves a solubility less than that referred to in our Vol. I. Heat was in consequence employed to effect solution. Crystals were deposited which were unlike Aspirin. He draws attention to the literature, which conveys that Aspirin is split up *in proportion to time* in such a case, one worker having suggested that Potassium Acetyl-Salicyl-oxonium Acetyl-Salicylate may be formed. We, of course, agree with the conclusions that heat should be avoided in such instances and the prescriber should modify such a prescription, for example, to :—

R

Aspirin	2 drachms
Potassium Citrate	.		4 drachms
Water to	6 ounces.

This is well within the 1 in 20 limit we have mentioned.

We made up the mixture referred to by Wilson—Aspirin 3 drachms, Potassium Citrate 6 drachms, and water to 6 ounces—employing heat to 60° C., and found we could extract a compound with the characters of Aspirin from it on cooling, using either Ether or Chloroform. Such solutions appear to us to be of the 'balanced' type, which will decompose in proportion to time.

An additional bottle, using 3 drachms, etc., and heating to 60° C., was made 6-3-29 and kept until 20-4-29. The crystals separated had the characters of Aspirin.

D. B. Dott (P.J. i./29,302) gives an account of three experiments which he conducted by adding varying quantities of Aspirin to different amounts of Sodium Bicarbonate in two cases and to Sodium Carbonate in a third case, and after standing for a little time adding HCl and extracting with Ether or Ether-Chloroform. These experiments showed that the degree of decomposition when the reaction had been going on for 2 hours was relatively slight.

In a further note (P.J. i./29,355) he records two experiments in which the mixtures are left for 4 hours and 24 hours. In the first instance 5.27% Salicylic Acid was recovered and in the second 14.4%.

We deal *antea* with the hydrolysis of Aspirin in *Plain Water* at 35° C. in various periods of time.

ACIDUM SULPHURICUM.

Sulphuric Acid is used in manufacture of glucose which is employed in making beer. Owing to it being made from Pyrites, it contaminated the glucose and thence the beer with arsenic in 1900. *Vide also Arsenium.*

Sulphur Dioxide and Trioxide in large quantities are detrimental to health, metal fittings, furniture, etc. During the carbonization of coal the gas that is evolved carries away with it large quantities of Sulphur, mostly in the form of Sulphuretted Hydrogen. Carbon Bisulphide and certain other Sulphur compounds are present in small proportions. In the purification of gas the whole of the Sulphuretted Hydrogen is removed and a certain amount of the other Sulphur compounds. All that remains in the gas as supplied to the public is about 30 grains of Sulphur—mainly in the form of CS₂—per 100 cubic feet.

Prior to 1906 Parliamentary restriction prevented the presence of more than 20 grains of Sulphur per 100 cubic feet, but this restriction was removed and regarded as unnecessary. The Sulphur contained in the gas supplied to the public contains only 3% of the Sulphur present in the original coal, so that the substitution of gas for coal must necessarily diminish to a negligible quantity the pollution of the air with sulphurous gases.

The following figures for Sulphur contained in the gas of the three principal London Gas Companies are given in the Annual Report of the L.C.C. for the year 1927.

Company.		Sulphur in grains per 100 c. ft. of gas.
Gas Light and Coke Co.	26.1
South Metropolitan Gas Co.	20.0
Commercial Gas Co.	27.5

Sulphuric Acid Manufacture, Theory of Reynolds and Taylor.—P.J. i./12, 486.

Volatility of Sulphuric Acid when used in a vacuum desiccator has been found to be quite perceptible.—P.J. ii./13, 497.

Sulphuric Acid, Solidified.

Sulphuric Acid mixed with 25% to 30% Kieselguhr becomes completely solid—suitable for transport.—P.J. i./13, 206.

Sulphuric, Nitric and Nitrous Acids in admixture, Determination of.—P.J. i./13, 469.

ACIDUM SULPHUROSUM.

Sulphurous acid is a strong reducing agent. For example, many colours are bleached by the sulphurous acid combining with the oxygen of any water present, hydrogen being liberated, which latter forms colourless compounds with the colours. These compounds may then be removed by washing.

The gas compressed in small cylinders was used for **Room Disinfection**, but Formalin (*q.v.*) is more used now.

"**Clayton Gas**," consisting principally of the residual nitrogen of the air, sulphurous acid up to 15%, and a considerable amount of sulphuric acid (which is useful, as it renders the gas visibly opaque) has been employed for freeing ships' holds from vermin. A special apparatus is used.

Calcil Bisulphis. Is an antiseptic supplied in solution. Checks fermentation and putrefaction. Has been employed for preserving foods. ("Madame Rachel").

Calcium Sulphite, CaSO_3 , = 120.134. A white powder, soluble in dilute Sulphurous Acid, has similar properties in less degree.

ACIDUM TANNICUM.

The identification by chemical methods of drugs containing Tannins.—A. H. Ware, P.J. ii./25, 131.

A review of the Tannins in astringent drugs of the *B.P.*—A. H. Ware, P.J. ii./26, 162.

Commercial examination of by comparative methods.—W. B. Forbes, per Y.B.P./26, 293.

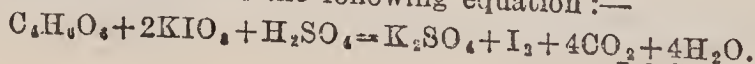
Ammonium Molybdate 10% solution gives a reddish-brown colour with Tannic Acid, also Gallic Acid, Pyrogallol and Tinct. Catechu. May be used for colorimetric assay for Tannin and drugs containing it.—J. Rae, P.J., i./28, 539.

ACIDUM TARTARICUM.

Detection in syrups and lemonades. Dilute 100 Cc. of the liquid with 20 Cc. water and filter into 300 Cc. test-glass. Add 20 Cc. strong solution of Calcium Acetate, made by dissolving CaCO_3 32 Gm. in Glacial Acetic Acid 120 Cc. and diluting to 1 litre with distilled water. Mix, stir well, and set aside for 72 hours. In presence of Tartaric Acid an evident crystalline deposit will be seen which is identified by micro-examination. Confirm by applying Denige's Test (Resorcin and Sulphuric Acid).—per Y.B.P.'26, 179.

Estimation of Tartaric Acid.

About 0.3 Gm. of the acid is added to a flask containing 1 Gm. of Potassium Iodate, a few drops of water and 30 Cc. concentrated Sulphuric Acid, and the mixture is heated for about 30 minutes, until most of the Iodine is expelled. Water is added and the last traces of Iodine are removed by boiling. By estimation of the remaining Potassium Iodate (by adding Potassium Iodide to an aliquot portion and titrating with Thio.) the amount of Tartaric Acid can be calculated from the following equation:—



J.C.S., A. ii. 24, 73.

Estimation of Lead in Tartaric Acid.

Best English tartaric acid as a rule does not contain more than 5 parts per million of lead and rarely exceeds 10. Foreign acids contain more.

Prepare a standard lead nitrate solution in water 0.4 Gm in 250 Cc. This should be kept distinctly acid, and is diluted 100 times for use. 1 Cc. of this diluted solution contains 0.00001 Gm. Pb. 7 Gm. of tartaric acid are dissolved in 50 Cc. of water in a Nessler glass with internal diameter 2.5 Cm., and in another 2 Gm. of the same acid are dissolved in the same amount of water. To the first, ammonia is added in excess, and a few drops of a 10 per cent. potassium cyanide solution are added to prevent the iron and copper from interfering with the sodium sulphide solution which is then added to the first Nessler glass.

The amount of lead solution added to the 'dummy' to match the colour of the solution of the sample on adding sulphide is the amount present in 5 Gm. of the sample. One arrives, therefore, at the amount of lead present in parts per million; e.g., 5 grammes of acid requiring 5 Cc. of diluted standard lead solution to balance coloration represent a content of 10 parts per million. Do not add lead solution after the sodium sulphide, this is a grave source of error.

To eliminate the inherent colour of the solution of the substance before adding the sulphide it may be necessary to add a minute quantity of burnt sugar to the 'dummy'.

If the sample be rich in lead, use correspondingly less of it, e.g. 2 Gm.

Method of Producing Lead-free Tartaric Acid.—Where the proportion of lead is excessive (e.g. 40 parts per million), pure lead-free acid for use as 'dummy' will be necessary. To prepare this 250 Gm. of the best acid obtainable are placed in a strong bottle fitted with rubber cork, and 1000 Cc. cold saturated hydrogen sulphide solution are added to nearly fill the bottle, which is (cautiously) then well shaken to dissolve the acid. Great internal pressure is produced owing to comparatively slight solubility of hydrogen sulphide in solutions of citric or tartaric acid. Allow to stand one day, filter, evaporate and crystallise. The solution on concentrating may become straw-coloured, which can be removed by stirring into the hot solution a crystal of sodium chlorate. The first crop of crystals equal to half the acid taken will be absolutely lead-free.—C. Alex. Hill, C.D. March 15, 1905.

Minute amounts of Lead and Arsenious Oxide below 0.002 (= $\frac{1}{50}$ grain per lb.), and 0.00014% ($\frac{1}{100}$ grain per lb.) respectively, would not justify condemnation.—B.M.J. ii./07, 1140, cf. also Arsenium Chapter.

Lead should not exceed 10 to 20 parts per million.

B.P. '14 requires not exceeding the latter figure and 1.4 per million Arsenic.

Acidum Glutaricum. Syn. n- PYROTARTARIC ACID.



Isomeric with Methyl-Succinic, Ethyl-Malonic and Dimethyl-Malonic. Acids, four isomers being possible. Colourless crystals,—soluble in water and alcohol. M.Pt. 97° C.

ACONITI RADIX.

The B.P.'14 does not give any support to British cultivation of plants. In the case of Aconite the cheap imported plants can be used and even if the alkaloids of foreign aconite consist chiefly of Aconine there is nothing to prevent its use, as the work requires only a certain percentage of alkaloids without defining.—E. M. Holmes, P.J. i./15, 5.

Assay experiments using the drug purposely spoilt by damp and allowed to go fungoid. Also results with old sample; of the drug showed that the alkaloidal content is a distinct indication of the value corresponding with physiological test results. In the first case, e.g., the alkaloidal content was 0.66% before and 0.3% approx. after spoiling. Aconite properly kept will not deteriorate. When deterioration is due to heat the weight of Ether-soluble residue is increased, the basic properties decreased, hence the deterioration is easily detected by volumetric assay. Chloroform should not be used in the assay.—P.J. ii./11, 33.

Farr and Wright found in Aconite Extract an average of 0.43% total alkaloid. The amount in the root is about twice that of the leaf. They found in dry root extract from 1.2 to 6%, English root being the best. A method of making the extract is outlined. The average yield of the dry extract was 25.9%, the Ether-soluble alkaloid in this averaging 1.95%. Foreign root yielded 30% with an average of only 0.68% Ether-soluble alkaloid. A standard of 1% proposed. The dose of this Extract would be $\frac{1}{8}$ to $\frac{1}{4}$ grain. Foreign root is very mixed owing to mode of collection.—P.J. i./13,216.

Aconite Extract Assay. Total Ether-soluble Alkaloid method and those which involve the effect of the partition coefficient between the immiscible solvents Ether and water. The methods are not interchangeable.—C. W. Cornwall and A. J. Jones, P.J. ii./26,197; C.D. ii./26,238.

Aconite Tincture and Liniment Assay.—Loss of time caused by filtering the acid liquid can be got over thus:—

Evaporate 15 Cc. of Liniment or 100 Cc. of Tincture at low temperature to remove bulk of the alcohol. Add 5 Cc. of 10% Sulphuric Acid. Shake with 20 Cc. Petroleum Ether, rinse same with water and extract with Ether after making alkaline. Evaporate the Ether extracts and titrate.—E. J. Chappel & N. L. Allport, B.P. Conf., 1920.

Ammonium salts can be decomposed by alkaloids (e.g., Atropine, Aconitine and Strychnine) in favourable circumstances—may produce error in titrating residues. The power of expelling ammonia in this way is possessed probably by all alkaloids.—P. A. W. Self, P.J. i./15,585.

ACONITINA.

Schulze's formula (found in 1906) is $C_{34}H_{47}NO_{11}$ and is more generally accepted than the B.P. '14 formula.

FR. CX. gives tests for distinguishing pure aconitine from decomposition products and substances which occur with it in the root.

Aconitine (like Hyoscine) is resistant to putrefaction.—cf. P.J. ii./20,222.

Pseudoaconitine.—A crystalline alkaloid obtained from Indian (or Nepaul) aconite, *A. laciniatum* melts at $201^{\circ}C$. and has the constitution of acetyl-veratryl-pseudoaconine.

Neopeltine.—A new amorphous alkaloid has been isolated from *Aconitum Napellus*.—J.C.S., A. i./25,283.

Most of the Japanese Aconite plants contain several isomers and closely related Aconitines. Methods of extraction and isolation of 6 isomers.—Y.B.P./25,48,49.

ETHER.

Historical.—Some doubt seems to exist as to who actually used ether first. Previously we stated W. T. G. Morton was the first administrator, —Oct. 16th, 1846, at the Massachusetts General Hospital. Haydn's Dict. of Dates states Dr. C. J. Jackson, of Boston, first gave it for insensibility to pain, and directed Morton in its first use in surgery. Now it appears the credit is due to Crawford Williamson Long, who first administered ether as an anæsthetic to his patient, Mr. William Venable, on March 30th, 1842, in Jeffersonville, Georgia.

Ether made from Methylated Spirit yields a proportion distilling below 34° due to the **Methyl Oxide** formed from the Methyl Alcohol. There is no objection to the Methyl Oxide when the Ether is used for local anæsthesia. The B.P. '14 test for Methyl compounds in Purified Ether says 'no fuchsin tint in 20 minutes.' This is satisfactory if by violet colour a slight of the least quantity of formaldehyde causes a marked violet. The purest Ether, however (even from Rectified Alcohol) gives a faint indigo blue in the time—this must not be confused.—D. B. Dott, C.D., Feb. 20/15.

A sample of ordinary 0.720 ether from S.V.M. gave nearly 24 parts of **Acetone** per 10,000.

As a *qualitative* test **Rothera's Nitro-Prusside Test** may be used. 5 Cc. of Ether, 1 Cc. of 5% Sodium Nitro-Prusside solution and 3 Cc. of Strong Ammonia are shaken together. Then solid Ammonium Chloride is added, *q.s.* to supersaturate and the whole shaken. Samples will show a slight reaction or none at all.—A. J. Jones, B.P. Conf., 1919.

Ordinary Methylated Ether in our experience gives coloration with this test.

Scott Wilson's Reagent.—Dissolve Mercuric Cyanide 0.5 Gm. and Sodium Hydroxide 9 Gm. in water 60 Cc., and add with constant stirring 20 Cc. of 0.727% Silver Nitrate solution. No turbidity should develop on shaking the ether with excess of the reagent.

Methyl Compounds, Formaldehyde and Acetone in Purified Ether.—A. J. Jones, B.P. Conf., 1919.

The substitution of Normal Sulphite for Sodium Bisulphite in the B.P. test is essential for detection of Methyl compounds in Ether.—D. B. Dott, P.J. ii./23,661. Also P.J. i./24,47 and 177.

For quantitative determination employ Scott Wilson's method.—Jl. Physiol., XLII., p. 444.

Ethylenic Derivatives.

Denigé's Reagent, consisting of 50 Gm. Mercuric Oxide dissolved in a mixture of 200 Cc. concentrated Sulphuric Acid and 1 litre of water, is shaken with an equal volume of Ether and set aside for one hour. No white opalescence should be produced in the aqueous layer, as this, slowly changing to a yellow precipitate, indicates the presence of ethylenic derivatives.—J.C.S., A. ii./23,587.

Peroxides in Anæsthetic Ether.

The exclusion of light is the most important factor on the rate of formation of peroxide. Amber bottles are suitable. The most effective substance for retarding the formation of peroxide is shown to be **Pyrogallol** (0.01 per cent.).—G. Middleton, B.P. Conf., 1924.

JORRISON'S REAGENT (0.4 Gm. Vanadic Acid in 4 Cc. of Sulphuric Acid and 96 Cc. Water) gives a red colour with Ether if peroxides are present. Aldehydes and unsaturated alcohols give a blue color on keeping.—J.C.S. A.ii./24,706.

Ferrous Thiocyanate Test.

The presence of Peroxides can be shown as follows. To Ether 5 Cc. add N/10 Potassium Thiocyanate solution 1 Cc. and 1 drop of fresh 5% Ferrous Ammonium Sulphate solution. If Peroxide be present a pink or red tint develops almost immediately.—F. H. Hocking, per C.D. i./27,592. *See also* Y.B.P./24,615.

We found commercial samples (1929) to respond as follows :

ETHER. SULPH. METH. .720 gave a decided reaction.

„ B.P. METH. .720, 'For anæsthesia,' gave a slight reaction.

„ 'ABSOLUTE' .720, 'For anæsthesia,' gave no reaction.

The test, we determined, is sensitive to 1 part H_2O_2 per million.

Two simple tests for detection of Aldehyde (Ammoniacal Silver Nitrate) and Peroxides (Phenolphthalein and Potassium Iodide).—E. B. Robinson, L. i./28,856.

Of 100 anæsthetic Ethers tested, 34 were seriously contaminated, Peroxide and Aldehyde being the chief contaminants, the former sharply predominating. The time of storage a probable factor in determining oxidation.—Per Y.B.P./25,152.

The following tests are suggested in **P. Helv. V.** for purity of anæsthetic Ether: It should give no colour, nor more than slight opalescence with Nessler's Reagent. 1 Cc. floated on a mixture of 1 drop Stamm's Phenolphthalin Reagent, 2 Cc. very dilute $CuSO_4$ solution and 2 Cc. water, should show no pink ring at zone of contact, either at once or after 30 minutes.—Per Y.B.P. 25,298.

STAMM'S PHENOLPHTHALIN REAGENT. Boil Phenolphthalein 1 Gm. with water 20 Gm., NaOH 10 Gm., and Zinc Dust 5 Gm., till solution is colourless. Dilute with water to 50 Cc. and filter through asbestos. Mix 1 drop of this

solution with 1—2 drops of CuSO_4 solution (1 : 2000) and add $\frac{1}{2}$ to 1 Cc. of Ether to be tested. If Peroxides are present a ring, pink to intense red, is formed at zone of contact. **Anæsthetic Ether should be stored in brown bottles covered with black paper**—brown bottles alone are not sufficient protection.—per Y.B.P./26,173.

Powdered Iron, 1 Gm. per 100 Cc. of freshly distilled Ether, prevents formation of Peroxides.—P.J. ii./27,434.

ÆTHERIS NITROSI SPIRITUS (B.P. '14).

Estimation—5 Cc. of this Spirit treated with 5 Cc. of Potassium Iodide Solution and 5 Cc. of Dilute Sulphuric Acid yield at least 20, but not more than 35 Cc. of Nitric Oxide, corresponding to 1.52 to 2.66% by weight of Ethyl Nitrite, Iodine being liberated.

Ammonium Acetate or Citrate hinders the deterioration of Spirit of Nitrous Ether.—D. J. Leech.

This preparation kept under the best conditions undoubtedly decomposes.

The first change is probably the formation of aldehyde and nitrous acid, thus :



Then the aldehyde is oxidised into acetic acid.

In the course of time the nitrous constituent of the spirit entirely disappears, but aldehyde, one of the most readily oxidisable bodies, remains.

The spirit should be kept in cool cupboards and in well-filled bottles, kept preferably upside down.

With regard to the 'volatilisation' of Ethyl Nitrite, Cowley has shown that every trace of Ethyl Nitrite disappears from a solution within a few days in ordinary vessels. As to decomposition in an *Aqueous Solution*, a mixture containing Spirit of Nitre loses the whole of it in three days. With regard to decomposition in *Alcoholic Solution*, this is of such varied character that it is impossible to represent by an equation, though the following appears to be preliminary :



Solutions in Absolute Alcohol change less rapidly than those in 90% Alcohol on account of the Water present. A mixture of 90% Alcohol and Glycerin in equal volumes is a good solvent for all preparations of Ethyl Nitrite.

ALCOHOL.

The strength of Alcohol is usually expressed in terms of Vol. % though the Board of Customs and Excise favours 'proof' terms. Rebate Claims on Immature Spirit must be made in terms of proof gallons and hundredths of a proof gallon.

Alcohol Dilution Rules.

If V be the volume percentage of the stronger alcohol and v of the alcohol required—

I. *By volume.* Mix v volumes of the stronger alcohol with distilled water, *q.s.*, after cooling to make V volumes, *e.g.* to make an alcohol 43% from alcohol 95% take 43 volumes of the 95% and make up to 95 volumes.

II. *By weight.* Proceed on the same lines by weight throughout.

To Transpose Volume per cent. of Alcohol into Weight per cent. The volume per cent. is multiplied by 0.7938, and the product divided by the Sp. Gr. of the liquid, *e.g.*, $\frac{80.22 \text{ V per cent.} \times 0.7938}{0.863} =$

73.7875 weight per cent. To express the Weight per cent. as Volume per cent. divide the weight per cent. by 0.7938 and multiply

by the Sp. Gr. of the liquid, *e.g.*, 90.29 per cent. by weight =

$$\frac{90.29 \times 0.822}{0.7938} = 93.49 \text{ V per cent.}$$

To state Volume per cent. as Alcohol of Proof Strength. Multiply V per cent. by 1.753 and deduct 100 from the product. Thus 65 V per cent. = $65 \times 1.753 - 100 = + 13.945^\circ$ over proof. Further, alcohol of 25 V per cent. = $25 \times 1.753 - 100 = - 56.175^\circ$ proof, *i.e.*, 56.175° under proof.

(B.P., 1885, stated: Proof spirit = about 57 per cent. alcohol by vol., *i.e.*, 57 parts alcohol with water produce 100 parts proof spirit.)

\therefore 1 part alcohol will make $\frac{100}{57} = 1.753$ (about) parts proof strength.

Conversely to state Alcohol of Proof Strength as Vol. per cent.:—

Add 100 to the proof strength and divide the product by 1.753 ; thus,

$$13.945^\circ \text{ o.p.} = \frac{113.945}{1.753} = 65\% \text{ by vol., and}$$

$$56.175^\circ \text{ u.p.} = \frac{100 - 56.175}{1.753} = 25\% \text{ by vol.}$$

To Convert Proof Gallons to Bulk Gallons multiply by:—

$$\frac{\text{Proof Strength} + 100}{100}$$

100 Vols. of Alcohol 90% (approx. 58° o.p.) are equivalent to 158 Vols. of Proof Spirit.

“Proof Spirit” has Sp. Gr. 0.920. This, in the olden time, was found to be the weakest spirit that could be put to the proof of igniting a little gunpowder moistened with it. If the spirit caught fire and inflamed the gunpowder, it was designated “over proof,” and if not, “under proof.” By the Hydrometer Act, 58 Geo. III. cap. 23, Proof Spirit is defined as spirit of strength, which at a temperature of 51° F. weighs exactly twelve-thirteenths of an equal quantity of distilled water.

Laws governing the Molecular combination of Alcohol with Water. —P.J. i./10,754.

The following Table, founded on B.P. 1898 and Gilpin’s Tables, shows:—

(i.) The volume of Distilled Water necessary to be added to 100 volumes of Alcohol (90%) for the production of each strength of Diluted Alcohol.

(ii.) The volumes of Alcohol (90%), and of Distilled Water respectively which, when mixed and reduced to 60° F. (15.5° C.), will produce, allowing for contraction in volume, 1,000 Cc., 1 pint, or 1 gallon of each strength of Diluted Alcohol.

The Specific Gravity and the exact Excise (Sikes’) strength at 60° F. (15.5° C.), in degrees over proof (O.P.) and under proof (U.P.), of each dilution, are given in the first column.

TABLE FOR THE DILUTION OF ALCOHOL (90%) TO WEAKER STRENGTHS.

Volume Percentage, Specific Gravity, and Excise Strength	Alcohol. (90 per cent.)	Distilled Water.	Volume Produced.
70 per cent. Sp. Gr. 0·8900 22·7° O.P.†	100 vols. + 31·05 vols. 777·8 Cc. + 241·6 Cc. *648·5 Gm. + 241·6 Gm. 15 oz. 266 m. + 4 oz. 398 m. 124 oz. 215 m. + 38 oz. 307 m. *6 lbs. 7½ oz. + 2 lbs. 6½ oz.	= 128·57 = 1000 Cc. = 1000 Cc. = 1 pint = 1 gal. = 8 lbs. 14½ oz.	
60 per cent. Sp. Gr. 0·9135 5·20° O.P.†	100 vols. + 53·65 vols. 666·7 Cc. + 357·8 Cc. *555·9 Gm. + 357·8 Gm. 13 oz. 160 m. + 7 oz. 74 m. 106 oz. 320 m. + 57 oz. 112 m. *5 lbs. 9 oz. + 3 lbs. 9½ oz.	= 150 = 1000 Cc. = 1000 Cc. = 1 pint = 1 gal. = 9 lbs. 2½ oz.	
45 per cent. Sp. Gr. 0·9436 21·2° U.P.†	100 vols. + 105·34 vols. 500 Cc. + 526·6 Cc. *417·2 Gm. + 526·6 Gm. 10 oz. + 10 oz. 256 m. 80 oz. + 84 oz. 130 m. *4 lbs. 2½ oz. + 5 lbs. 4½ oz.	= 200 = 1000 Cc. = 1000 Cc. = 1 pint = 1 gal. = 9 lbs 7 oz.	
20 per cent. Sp. Gr. 0·9760 64·9° U.P.†	100 vols. + 355·8 vols. 222·2 Cc. + 790·7 Cc. *185·2 Gm. + 791 Gm. 4 oz. 213 m. + 15oz. 390 m. 35 oz. 267 m. + 126 oz. 243 m. *1 lb. 13½ oz. + 7 lbs 14½ oz.	= 450 = 1000 Cc. = 1000 Cc. = 1 pint = 1 gal. = 9 lbs. 12½ oz.	

NOTE.—*These figures are the WEIGHTS necessary to produce a gallon and a litre respectively, at 15·5° C. † Stevenson.

Detection of Methyl Alcohol.—Place in a 100 Cc. Erlenmeyer flask, as a check, Sodium Salicylate 0·5 Gm. and pure Alcohol 1 Cc., and into a similar flask Sodium Salicylate 0·5 Gm. and 1 Cc. of the Spirit to be tested. To both flasks add twenty drops of Sulphuric Acid in four parts at an interval of one minute. If Methyl Alcohol is present, an odour of Methyl Salicylate is developed.

Our experiments showed (July 1920) that a distinct odour of Methyl Salicylate is obtainable with a 1% admixture of Methyl Alcohol in S.V.R.

U.S.X. test for Methyl Alcohol (Methanol):—Dilute the spirit so that it contains about 50% by volume of Ethyl Alcohol. Place 5 Cc. of this dilution in a test-tube, add 2 Cc. of 3% Potassium Permanganate solution and 0·5 Cc. of Phosphoric Acid. Allow to stand 10 minutes. Add 1 Cc. of 10% Oxalic Acid solution and allow to stand until the liquid is a transparent brown. Then add 5 Cc. of a diluted and cooled Sulphuric Acid, made by mixing 3 vols. of distilled water and 1 vol. of Sulphuric Acid. Add 5 Cc. of freshly made Fuchsin-Sulphurous Acid solution. Mix and observe after 10 minutes. It may have a reddish or pale green tint against a white background, but not a distinct blue or violet colour.

Fuchsin Sulphurous Acid Test is made thus:—

Dissolve Fuchsin 0·2 Gm. in 120 Cc. hot distilled water, cool, and add a solution of Anhydrous Sodium Sulphite, 2 Gm. in 20 Cc. of water and 2 Cc. of strong Hydrochloric Acid. Dilute to 200 Cc. and allow to stand 1 hour before use. To be recently prepared.

This test for Methyl Alcohol, in which it is oxidised to Formaldehyde is the best one.—B.C.A./28, A.1113.

The original Schiff's Reagent for Aldehydes was 0·025% of Fuchsin decolorised with SO₂.

We have found the Methyl Salicylate test (above) quite distinctive.

ETHYL ALCOHOL TABLE.

As employed in the Government Laboratory.

Sp.Gr. at 15.5°C.	Wt. per cent.	Vol. per cent.	Sp.Gr. at 15.5°C.	Wt. per cent.	Vol. per cent.	Sp.Gr. at 15.5°C.	Wt. per cent.	Vol. per cent.	Sp.Gr. at 15.5°C.	Wt. per cent.	Vol. per cent.
0.999	0.53	0.66	0.947	36.00	42.95	0.895	60.23	67.92	0.843	82.00	87.09
0.998	1.07	1.34	0.946	36.54	43.54	0.894	60.66	68.33	0.842	82.40	87.42
0.997	1.61	2.02	0.945	37.07	44.13	0.893	61.09	68.74	0.841	82.80	87.74
0.996	2.17	2.71	0.944	37.60	44.71	0.892	61.52	69.14	0.840	83.20	88.06
0.995	2.73	3.42	0.943	38.12	45.28	0.891	61.95	69.55	0.839	83.60	88.37
0.994	3.31	4.14	0.942	38.64	45.85	0.890	62.38	69.95	0.838	83.99	88.68
0.993	3.90	4.88	0.941	39.15	46.40	0.889	62.81	70.35	0.837	84.39	88.99
0.992	4.51	5.63	0.940	39.65	46.95	0.888	63.24	70.75	0.836	84.78	89.30
0.991	5.13	6.40	0.939	40.15	47.50	0.887	63.67	71.15	0.835	85.17	89.61
0.990	5.76	7.18	0.938	40.65	48.04	0.886	64.10	71.55	0.834	85.56	89.91
0.989	6.41	7.98	0.937	41.15	48.57	0.885	64.53	71.95	0.833	85.95	90.22
0.988	7.08	8.80	0.936	41.64	49.10	0.884	64.96	72.34	0.832	86.34	90.52
0.987	7.76	9.65	0.935	42.13	49.63	0.883	65.39	72.74	0.831	86.73	90.82
0.986	8.46	10.51	0.934	42.62	50.15	0.882	65.81	73.13	0.830	87.11	91.11
0.985	9.18	11.40	0.933	43.11	50.67	0.881	66.24	73.52	0.829	87.50	91.40
0.984	9.91	12.29	0.932	43.59	51.18	0.880	66.66	73.91	0.828	87.88	91.69
0.983	10.65	13.20	0.931	44.06	51.68	0.879	67.09	74.30	0.827	88.27	91.98
0.982	11.42	14.13	0.930	44.53	52.18	0.878	67.51	74.68	0.826	88.65	92.26
0.981	12.20	15.08	0.929	45.00	52.67	0.877	67.93	75.06	0.825	89.03	92.55
0.980	12.99	16.04	0.928	45.47	53.16	0.876	68.35	75.44	0.824	89.41	92.83
0.979	13.80	17.02	0.927	45.94	53.65	0.875	68.77	75.82	0.823	89.79	93.11
0.978	14.61	18.00	0.926	46.40	54.14	0.874	69.19	76.19	0.822	90.16	93.38
0.977	15.43	18.99	0.925	46.87	54.62	0.873	69.62	76.57	0.821	90.53	93.65
0.976	16.25	19.98	0.924	47.33	55.10	0.872	70.04	76.94	0.820	90.90	93.92
0.975	17.08	20.97	0.923	47.79	55.58	0.871	70.46	77.32	0.819	91.27	94.19
0.974	17.90	21.96	0.922	48.25	56.05	0.870	70.88	77.69	0.818	91.63	94.45
0.973	18.72	22.94	0.921	48.71	56.52	0.869	71.30	78.06	0.817	92.00	94.71
0.972	19.53	23.91	0.920	49.17	56.99	0.868	71.72	78.43	0.816	92.36	94.97
0.971	20.34	24.85	0.919	49.63	57.46	0.867	72.14	78.80	0.815	92.72	95.22
0.970	21.14	25.83	0.918	50.08	57.92	0.866	72.55	79.17	0.814	93.08	95.47
0.969	21.93	26.77	0.917	50.53	58.38	0.865	72.97	79.53	0.813	93.44	95.72
0.968	22.71	27.69	0.916	50.98	58.83	0.864	73.39	79.89	0.812	93.80	95.97
0.967	23.48	28.69	0.915	51.43	59.29	0.863	73.81	80.25	0.811	94.15	96.21
0.966	24.23	29.48	0.914	51.88	59.74	0.862	74.22	80.61	0.810	94.50	96.45
0.965	24.97	30.34	0.913	52.33	60.19	0.861	74.64	80.97	0.809	94.85	96.69
0.964	25.63	31.18	0.912	52.77	60.63	0.860	75.05	81.32	0.808	95.20	96.93
0.963	26.37	31.99	0.911	53.21	61.07	0.859	75.47	81.68	0.807	95.55	97.16
0.962	27.06	32.79	0.910	53.65	61.51	0.858	75.88	82.03	0.806	95.89	97.39
0.961	27.73	33.56	0.909	54.10	61.95	0.857	76.30	82.38	0.805	96.23	97.62
0.960	28.39	34.33	0.908	54.54	62.39	0.856	76.71	82.73	0.804	96.57	97.84
0.959	29.03	35.06	0.907	54.98	62.83	0.855	77.12	83.08	0.802	96.91	98.06
0.958	29.66	35.79	0.906	55.42	63.26	0.854	77.53	83.42	0.802	97.25	98.28
0.957	30.28	36.50	0.905	55.87	63.70	0.853	77.94	83.77	0.801	97.59	98.49
0.956	30.90	37.20	0.904	56.31	64.13	0.852	78.35	84.11	0.800	97.91	98.70
0.955	31.50	37.89	0.903	56.75	64.56	0.851	78.76	84.44	0.799	98.24	98.91
0.954	32.09	38.57	0.902	57.18	64.98	0.850	79.17	84.78	0.798	98.57	99.12
0.953	32.67	39.22	0.901	57.62	65.41	0.849	79.58	85.12	0.797	98.90	99.32
0.952	33.25	39.87	0.900	58.06	65.83	0.848	79.98	85.46	0.796	99.22	99.52
0.951	33.81	40.50	0.899	58.50	66.25	0.847	80.39	85.80	0.795	99.55	99.72
0.950	34.37	41.13	0.898	58.93	66.67	0.846	80.79	86.12	0.794	99.87	99.92
0.949	34.92	41.74	0.897	59.37	67.08	0.845	81.20	86.44	0.79359	100.00	100.00
0.948	35.46	42.35	0.896	59.80	67.50	0.844	81.60	86.77			

Methyl Alcohol Poisoning.—Symptoms differ from those of ordinary spirit in the marked muscular weakness and defective cardiac action which are followed by nausea, vomiting, coma or delirium of a much more intense and persistent character than those seen by ordinary intoxication.

Ethyl Alcohol undergoes complete combustion in the system, while perhaps Methyl is oxidised to Formic Acid and possibly Formaldehyde—both more or less toxic.—L. i./20,130.

METHYLATED SPIRIT DRINKING. Suggested addition of $\frac{1}{2}$ grain Tartar Emetic per ounce and a poison label.—F. S. D. Hogg, L. i./20,788.

In Glasgow the bars close at 12 noon on Saturdays so that the shipyard worker may take home his wages, but they reopen at 5. The drinking dens are crowded. The popular tippie is 'Biddie,' a deadly mixture of wine and methylated spirit. The red wine is bought at the less reputable bars at nine-pence a quart bottle; and the methylated spirit or 'feek,' as it is known here, is brought in and mixed with the so-called wine. The result is precisely the same as that seen in the New York drunkard.

'Red Biddie' is a devil's brew from a witch's cauldron. It makes the toper not so much drunk as doped. Glasgow police officers state that a man or a woman taken under the influence of 'Red Biddie' might lie unconscious for 24 hours, and at the end of that period, if they take a drink of water or any other liquid they immediately become drunk again.

They are like subjects under a hypnotic trance. In whatever position their limbs are placed so they remain.—R. E. Corder, *Daily Mail*.

Methyl and Wood Alcohols and Acetone are markedly more toxic than Ethyl Alcohol. Deleterious effects of chronic alcoholism on growth.—T. Sollmann, O. H. Schettler and N. C. Wetzler, *Jl. Pharm. and Exp. Therap.*, Nov., 1920. *Further details, Vol. I., p. 119.*

Aldehyde tests (P.G. VI.). The red colour of a mixture of 10 Cc. of absolute alcohol and 1 Cc. of potassium permanganate solution (1+999) should not turn to yellow within twenty minutes. On adding to a mixture of 10 Cc. of absolute alcohol, 10 Cc. of water, and 1 Cc. of silver nitrate solution (1+19), sufficient solution of ammonia to redissolve the precipitate at first thrown out, and then placing the mixture in the dark, no colouration or opalescence should occur within 12 hours. The latter test is modified in respect of Alcohol 90% in P.G.

U.S. IX. required that 10 Cc. with 5 Cc. of Liquor Potassæ (4.5%) shall not at once produce a yellow colour.

Acetone—Colorimetric method for determining and detecting in Spirit, based on formation of Indigo when Sodium Hydroxide is added to a mixture of o-Nitrobenzaldehyde and Acetone; can also be used for Isopropyl Alcohol after oxidation to Acetone.—C. A. Adams, P.J. ii./28,604.

Diethylphthalate detection in Alcoholic liquids.—per Y.B.P./25,151

AMOUNT OF ETHYLIC ALCOHOL BY VOLUME IN VARIOUS LIQUORS.

Whisky	51-59%	White Wine	12-14%
Rum		Champagne	10-13%
Gin		Orange Wine	10-12%
Strong Liqueurs		Burgundy	9-12%
Proof Spirit	57%	Hock	9-12%
Brandy	43-57%	Claret	8-12%
Port	20-30%	Cider	5-9%
White Wine (strong)	23-29%	Strong Ale or Stout	5-9%
Sherry	16-22%	Beer and Porter	2-5%
Madeira	16-22%		

—HALE WHITE.

The above are pre-war.

The current strengths are: Whisky, Rum, Gin and Brandy, 40-47%; Strong Liqueurs, 43-47%; Proof Spirit, 57.1%; Port, 16-22%; Sherry, 16-22%; Madeira, 16-22%; White Wine, 12-14%; Champagne, 10-13%; Orange Wine, 12-15%; Burgundy, 12-14%; Hock, 12-14%; Claret, 10-14%.

Mountain Dew Scotch Whisky. 40.1% Alcohol by volume, Total Extractives 0.15%, Ash 0.01%; Volatile Acidity (as Acetic) 19.4 per 100,000 of absolute Alcohol, Furfural 0.6 ditto, Esters (as Ethyl Acetate) 44 ditto, Aldehyde 22.5 ditto.—L. ii./23,1036.

British wines and temperance drinks. A few of the ordinary non-alcoholic wines were found to contain a little more than 2%. A sample of raspberry wine contained 3.28%.—G. C. Hancock, Min. Health Report, No. 24, B.M.J. i./24,1143.

P. Helv. gives a useful summary of analysis of wines.

Alcohol consumption in 1913 had fallen from 32 gallons of beer in 1900 per head to 27 and from 1.22 gallons of proof spirit to 0.67.—Prof. Wild. L. ii./20,52.

Some 40 or 50 abstracts of Patents and references to the production of Alcohol from materials other than the usual maize, potatoes, molasses, *e.g.* bananas, apple juice, chicory roots, peat, straw, currants, oil cake, etc., were found in the J.S.C.I., between 1893 to 1911. Sulphite Cellulose waste products said to be even more productive. The principle involved is the conversion of the cellulose into fermentable sugars.—Thomas Tyrer.—B. & C.D., May 26/11, 452; L. ii./10, 1924.

In the **Classen Process** for Alcohol production sawdust is digested with weak Sulphurous Acid in an autoclave under 90 to 100 lbs pressure, yielding a product containing 25% of sugar, 18% alkali or acid-soluble, and 56% insoluble carbohydrates. The solid Saccharine residue is a suitable spirit making material, but the Spirits Act, 1880, places such restrictions on the Spirit industry as to stop the progress.

A factory capable of treating 200 tons of sawdust per week could turn out between 300,000 and 400,000 gals. of proof spirit per annum. This would also give by-products of 50 tons acetic acid, 10 tons furfural, and 2,000 gals. of methyl alcohol for recovery. The spirit produced is of high quality, being free from fusel oil.—A. Zimmerman, C.D., Dec. 7/12.

SYNTHETIC ALCOHOL by these stages: Calcium Carbide \rightsquigarrow Acetylene \rightsquigarrow Acetaldehyde \rightsquigarrow Alcohol. Possible commercial success in Switzerland, L. ii./17, 250. From Ethylene extracted from Coal Gas, L. ii./19, 340 and L. i./20, 210.

Alcohol: its use and abuse.

Prof. W. E. Dixon thought it would be admitted that there was a growing world tendency towards temperance. Alcohol could be regarded as a food, in the sense that it spared the carbohydrates, fats and proteins. It has been said that Alcohol is a food surpassing Starch and Sugar in alimentary value, since weight for weight it contained more energy. It is a luxury and an expensive way of taking food, though it had yet to be proved that taken in strict moderation it had injurious effects. It was generally agreed by publicans that food was the solution of the problem of drunkenness—foreigners, including Jews, rarely got drunk because they ate while drinking. After 8 years' trial, the HARRISON NARCOTIC LAW had signally failed, due, he believed, to all the consideration being centred on the drugs and too little thought given to the nature of the addicts. **"Alcoholism" should be analogous with "Morphinism" and "Cocainism."** The alcoholic took alcohol because he needed it to become *normal*; he was a neurotic and if deprived of alcohol would take to drugs. Temperance measures should be taken with great circumspection. In America, since Prohibition, 255 deaths had been reported from poisoning by Methyl Alcohol and at least 100 cases of blindness due to Wood Alcohol. Numerous cases of eye injury reported from Denmark and Finland, due in the former to the purchase of substitutes owing to high cost of brandy, and in the latter to Prohibition. The answer to the Alcohol question was not Prohibition but Education. Sir Thomas Horder said that whatever Prohibition had, or had not, done in America, it had effected a great improvement in shutting up the 'gin palaces.' Prof. H. E. Armstrong pointed out that Science, by ensuring for Western Europe a safe water supply, had done much to eliminate the excessive use of Alcohol. Sir J. Crichton-Browne closed by quoting Prof. Starling to the effect that in a society like ours the abolition of alcoholic beverages would be a mistake, and if made compulsory, a national calamity.—B.M.J. i./24, 341.

Alcoholism in various social classes.—H. M. Vennor, L. ii./24, 109.

Alcoholism in relation to insanity and crime.—B.M.J. i./24, 523.

An examination of 1,300 prostitutes in Berlin before and in the early part of the war, showed that the proportion of Alcohol consumers was considerably higher among the healthy than among the consumptive, and that the heavier the drinker the more likely was pulmonary tuberculosis to be healed.—B.M.J. E. ii./24, 29.

Methynol, the German synthetic Alcohol, it is claimed, can be used for beverage purposes, as it has a 'kick,' but is not poisonous like Wood Alcohol. Largely imported into U.S.A.—P.J. i./25, 637.

Owing to the consumption of improperly refined distillates obtained from crude sorts of fermentations, 'the Alcohol question of to-day has become, from a medical standpoint, even more complex than it was in the pre-Prohibition period.'—Jl. A.M.A. ii./25, 1560.

Alcohol in the body.

The human body normally contains about 0.003% of Alcohol. Excess of 0.01% indicates that Alcohol has been taken recently. If analysis is made from 2 to 6 hours after taking Alcohol and the result multiplied by the body-weight it will give approximately the total of Alcohol taken. The presence of 0.4 to 0.5% represents a condition of drunkenness and means that about 300 Gm. of Alcohol has been taken—this would be present in about a pint of whisky—twice this amount will cause death.—Jl. A.M.A. ii./28,175.

LABORATORY PREPARATION OF ABSOLUTE ALCOHOL. May be obtained without distillation from ordinary spirit, 95 to 96%, as follows. Thoroughly cleanse small pieces of sheet Aluminium with pad of cotton and KOH solution: then rub with another pad moistened with HgCl_2 solution: wash with water and dry between filter paper. Immerse the activated Aluminium in the EtOH to be dehydrated. It first evolves H and then forms $\text{Al}(\text{OH})_3$, which is precipitated, and the EtOH becomes anhydrous. The activated foil retains its activity for a long period—if kept in a flask with a cork fitted with a Bunsen valve. Test Alcohol by dropping a little on to CaC_2 , when no odour of Acetylene should be perceptible.—per Y.B.P./27,179.

Mineralised Methylated Spirit. (Pyridinised). (See also Vol. I., p. 120.)

The B.M.A. in July, 1924, *protested against the use of Pyridine as denaturant as rendering the spirit unfit for surgical use with result that the Board of Customs and Excise permitted use of Industrial Methylated Spirit (i.e. unpyridinised) for medical and surgical purposes, other than internal use—under specific conditions as described in Vol. I. Older refs. on this matter in Vol. II., 18th Edn., pp. 25,26.*

METHYLATED SPIRITS AND ETHER REGULATIONS (NORTHERN IRELAND), 1928. In force from March 1, 1928.

Methylated Spirits. Retailers to keep records (in accordance with Schedules set out) of all purchases and sales. In the case of sales signature of purchaser and of introducer (if any) to be affixed, unless a signed order has been received, when the words 'Signed Order' must be entered with date of sale, the order endorsed with name of seller and date of sale and kept for 2 years. When selling to another retailer enter words 'Re-Sale.'

Methylated Ether. Wholesalers to keep records (in accordance with Schedule) of all sales of Ether and preparations, except proprietary medicines containing not more than 5%, and retailers authorised to sell such proprietary medicines; and preparations containing Ether, of formula sanctioned by Ministry of Home Affairs, or on prescriptions from medical men, dentists (marked "For local dental treatment only"), or veterinary surgeons (marked "For animal treatment only"), but may not supply more than once on same prescription. Prescriptions marked with date of dispensing and kept for 2 years. Permit may be granted to sell Ether for manufacturing or scientific use. Retailers to keep Register of all purchases and sales.—C.D., May 12, '28.

Ethyl Butyrate.— $\text{C}_3\text{H}_7\text{COO.C}_2\text{H}_5=116.096$. The chief constituent of Pine Apple Essence. A colourless liquid with Pine Apple odour Sp. Gr. 0.886 at 15° C. Miscible with Alcohol. Boiling pt. about 120° C.

Iso-Amyl Butyrate.

$\text{CH}_3.\text{CH}_2.\text{CH}_2.\text{COO.CH}_2.\text{CH}_2.\text{CH} < \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix} = 158.144$.

Colourless liquid with Sp. Gr. 0.882 at 0° C. Used as a flavouring agent.

Commercially the article contains 78 to 93%. Sp. Gr. ranged from 0.853 to 0.860. R.I. 1.4073 to 1.4110 at 20° C. B.Pt. about 135° C.

ALCOHOL ISOPROPYLICUM.

Isopropyl Alcohol, produced from Hydrocarbon gases, can be deodorised by treatment simultaneously with a hypochlorite and an oxidising agent—subject of a U.S. patent.

Isopropyl Alcohol made in Great Britain is obtained by catalytic reduction of Acetone. In perfumery, it is a good plan to blend with Ethyl Alcohol, the odour of the Iso—being too heavy and persistent when used alone. A table of solubilities of oils and synthetic perfumes in various spirits is given.—C.D., Jan., i./27,11 (ex P.R., July, 1923).

Detection. Distil 10 Cc., e.g. of Eau de Cologne with 20 Cc. of Potassium Bichromate solution and 1 Cc. of Sulphuric Acid in a 200 Cc. flask with caution and test for Acetone by the Nitroprusside Test. Industrial Methylated Spirit also gives the reaction but this gives colour with Sodium Nitroprusside before oxidation.—J. Rae, P.J. i./26,631.

Its presence may also be detected by the following reagent—which fails in the case of hydrocarbons. Mercuric Oxide (Red or Yellow) 50 Gm., Sulphuric Acid 200 Cc., Water 1 litre. A yellow precipitate indicates Isopropyl Alcohol when 3 drops of the reagent are heated with a few drops of the liquid. A white precipitate is formed by Acetone or Formaldehyde, but none is given by Methyl, Ethyl, and Amyl Alcohol or Ether.—P.J. ii./28,403.

Our findings (1929): *This reagent gives a yellow pp. with 75 to 100% Isopropyl Alcohol; white pp. with 50 to 75% and no pp. with further dilutions.*

Physiologically on the internal animal economy, it is comparable with acetone. It is oxidised to the latter in the organism. As a dehydrating agent it equals absolute alcohol and as a preservative agent and disinfectant it is superior.—H. C. Fuller, Chem. and Met. Engineering, Sept. 17'23.

No objection to its use where the quantity swallowed does not exceed a few Cc. at most. It is *not potable*.—P. H. Grant, J.A.M.A., '23,80,1341; Y.B.P. '23,361.

ALDEHYDUM FORMICUM.

Formaldehyde is an important raw material in the artificial silk industry and in the varnish and lacquer trades. Report of the Department of Scientific and Industrial Research on "The production of Formaldehyde by Oxidation of Hydrocarbons" (Chemistry Research, Special Rept., No. 1, H.M.S.O., 1927) —C.D. i./28,382.

Formalin as Preservative.

The addition of Formaldehyde to milk is prohibited by the Public Health (Milk and Cream) Regulations 1922, and by the Public Health (Preservatives in Food) Regulations 1925, *vide* Milk Analysis, and Vol. I., p. 127.

Determination of Formaldehyde—4 to 4½ Gm. of the solution (if about 40%) is accurately weighed into a stoppered flask of 150 to 200 Cc. capacity. About 50 Gm. of Ammonium Chloride in fine powder are next added and then 25 Cc. of a double Normal Solution of Caustic Soda,—flask is shaken meanwhile. Contents and flask are allowed to cool down to temperature of room, then 50 Cc. of Water, containing 4 drops of 1% Solution of Methyl Orange are added and titrated with Normal Sulphuric Acid. The number of Cc. of Normal Soda used, multiplied by 0.06 gives the weight of Formaldehyde. If the solution be acid another portion is titrated with decinormal alkali and phenolphthalein and the necessary correction made in the amount of Soda neutralised. *Cf.* also Estimation in Saponaceous Solutions, *infra*.

U.S.X. Method of Estimation is as follows:—

Transfer 3 Cc. of the solution of Formaldehyde to a tared flask containing 10 Cc. of distilled water. Stopper and weigh. Add 50 Cc. N/1 NaOH and then 50 Cc. H₂O₂ solution (10 vol.) previously neutralised with NaOH. Heat cautiously on the water bath 5 minutes, shaking occasionally. Allow to cool and titrate with N/1 H₂SO₄, using Litmus Solution. The U.S. solution shows not less than 37% HCOH, correction being made for acid if present. Each Cc. of N/1 NaOH = 0.03002 Gm. H.CO.H. Each Gm. of the U.S. Solution corresponds to not less than 12.3 Cc. of N/1 NaOH.

P. G. V. Method depended on reaction between Formaldehyde and Neutral Sodium Sulphite. The Bisulphite compound is formed and the Sodium Hydrate liberated is titrated with N/1 H₂SO₄ using Phenolphthalein as indicator:—



C. H. Hampshire and S. Furnival modified the P.G. process slightly as follows.—To 50 Cc. of freshly made Sodium Sulphite Solution (P.G. used 12½ Gm. of the crystalline salt in 50 Cc. of water), add a little Phenolphthalein and make solution colourless by carefully adding N. Sulphuric Acid. 1 Cc. of the Formaldehyde is then added and the mixture titrated at once with N/1 H₂SO₄ until the colour completely disappears. 1 Cc. of Acid = 0.030160 Gm. HCOH.

Samples of Formaldehyde Solution of commerce had Sp. Gr. from 1.0804 to 1.0886.

H.CO.H by weight 35.38% to 37.33% ; average 36.56%.

CH₂OH by weight 10.16% to 14.97% ; average 13.68%.

Presence of Methyl Alcohol prevents polymerisation but renders the solution liable to duty on basis of Ethyl Alcohol.

P. G. VI. Method is as follows : About 1 Gm. of solution accurately weighed is placed in 100 Cc. flask containing 2½ Cc. of water and 2½ Cc. of normal KOH. After shaking, make up to 100 Cc. volume. 10 Cc. of the solution is now mixed with 50 Cc. of N/10 Iodine and 20 Cc. of N/1 KOH added. After 15 minutes, add 10 Cc. of dilute Sulphuric Acid.

For every 0.1 Gm. of Formaldehyde solution, at least 23.3 Cc. of N/10 Iodine is required, so that for the saturation of the excess Iodine at most 26.7 Cc. of N/10 Sodium Thiosulphate are necessary. This represents a content of at least 35% Formaldehyde (1 Cc. of N/10 Iodine = 0.001501 Gm. of Formaldehyde, using Starch as indicator).

P.G.V. Method gives good results, but the end-point is not very sharp. 1% Thymolphthalein or Phenolphthalein in solution, saturated with NaCl gives better end-point.—per Y.B.P./26,174.

Formaldehyde Tablets. A colorimetric method of estimating Formaldehyde and para-Formaldehyde in tablets, using Schiff's reagent. The results obtained from commercial samples varied from 0.021 Gm. to 0.002 Gm. in commercial Formaldehyde and Menthol tablets weighing 0.791 and 0.69 Gm. respectively. An average content appears to be about 0.01 Gm.—N. Evers and C. M. Caines, B.P. Conf., 1921 ; P.J. i./21,499.

Poisoning from taking 300 Gm. of 40% Formaldehyde. Death in 6 hours.—P.J. i./24,555.

Meat Products. Detection of Formaldehyde. Direct application of H₂SO₄ + Fe or Voienet's Sodium Nitrite reagent gives characteristic violet reaction in presence of only a trace of Formaldehyde.—per Y.B.P./25,153.

Systematic tests for detection of Aldehyde.—E. C. Crocker, per Y.B.P./26,168.

Formaldehyde as food preservative—source of danger—S. Back, P.J. ii./24,289,308.

Production of Formaldehyde by intestinal bacteria. Schryver's Test the most delicate and reliable; to 10 Cc. of suspected solution add 2 Cc. 1% solution of Phenylhydrazine Hydrochloride, then 1 Cc. 5% Potassium Ferricyanide solution, and then 2 Cc. of concentrated Hydrochloric Acid—a pink colour appears if Formaldehyde is present (this colour soon fades, but is brought back, and intensified, by hydrogen peroxide). Table showing results of tests applied to various organisms. Test should be of considerable value in classification and identification of bacteria.—B. H. Shaw, B.M.J. i./24,461.

Histological use of Formaldehyde as preservative.—B.C.A./28,A1152.

ALKALOIDAL NOTES.

One drug may inhibit the action of another which normally produces a definite action in an animal, hence (1) the rates of adsorption differ, (2) a drug can no longer exert a certain action, if, on the site of this action, it is replaced by another drug. A point is made of the fact that when *alkaloids combine with substances in blood serum they do so very loosely*, since all the alkaloids can be regained by the simple means of either boiling or extraction by Ether.—W. S. van Leeuwen, Jl. Ph. and Exp. Ther., Vol. XXIV., '24,21. *The alkaloids when injected in form of their Salts are, we believe, first changed into their bases.*—See Vol. I., p. 132 et seq.

In a further paper, it is suggested that drug hypersensitiveness in man may be explained by the inhibitive action of normal blood serum, and the augmentative influences which a number of drugs, in extremely minute doses, exert on the stimulating action of other drugs. Reference is made to the idiosyncrasy of some persons towards Quinine, Veronal, Boric Acid, Antipyrine, Aspirin, and other drugs, and also to the observation that intravenous injection of Peptone or the intramuscular injection of milk will augment the pressure action of Adrenalin in cats and rabbits.—W. S. van Leeuwen, Jl. Ph. and Exp. Ther., Vol. XXIV., '24,25.

ALOES.

Extract Content in Aloes.

Average content water-soluble in Barbados Aloes was 60%, and in Socotrine Aloes 45% approx.

B.P. '14 requires loss on drying not more than 10%.

Anthraquinone derivatives other than Aloe-Emodin, Investigation to determine presence of. The results were negative. Aloe-Emodin was extracted by Petroleum Ether after distilling off an Essential Oil with steam. Both Cinnamic and *p*-Coumaric Acids were also obtained from the Aloes.—*F. Tutin and W. J. S. Naunton, P.J. ii./13,836.*

Characters and Tests of Aloin.

0.01 Gm. dissolved in 5 Cc. Water, 1 drop of Copper Sulphate Solution added and the mixture warmed, a red colour is produced—too much Copper spoils the colour.

The dry substance gives red colour with strong HNO_3 , but Aloin from Cape Aloes gives green. An aqueous solution shaken with Ether and the Ether layer separated and shaken with a little Caustic Potash, the latter becomes red—due to the small quantity of Oxymethylantraquinone present in Aloin.—*P.J. ii./10,235.*

AMMONIUM.

Ammonii Carbonas. On page 145 of Vol. I. data are provided of Self and Corfield's work conveying that a 1 in 8 solution was found to be stable. Experiments in the author's laboratory during 1929 showed that a 1 in 6 solution, which is commonly employed for dispensing, retained its Ammonia content for 3 months.

Ammonii Sulphocyanidum. *Syn.* AMMONII RHODANIDUM.— NH_4 CNS=76.112. White crystals soluble in Water and Alcohol. Reagent in toxicology to separate Arsenic, Antimony, Mercury, etc..

Recovery after taking 30 Gm. of pure Ammonium Sulphocyanide in 200 Cc. of Water.—*P.J. i./12,10.*

Hydrazine. *Syn.* DIAMIDE $(\text{NH}_2)_2$ =32.048. In the basic condition this body is not stable, but the Sulphate $(\text{NH}_2)_2 \cdot \text{H}_2\text{SO}_4$ is a well defined stable salt,—white crystals soluble in hot water. It is a useful reducing agent, *e.g.*, in making Colloidal Metal Hydrosols. It has antiseptic properties, *e.g.* it will destroy fungi, etc.

Photographic use.—Caldwell discovered that the inclusion of the salts of Hydrazine, or Hydroxylamine, in the emulsion renders a plate practically proof against over exposure or reversal. *Plates or papers treated with the Hydrazine Salts may also be printed right out and toned like ordinary P.O.P., or partly printed and the operation completed by development.*

AMYGDALA AMARA vel DULCIS.

Oleum Amygdalæ.

With regard to the results with Bieber's Test for adulterants *B.P.* '14 :—**APRICOT KERNEL OIL** gives a deep salmon red or peach blossom colour, changing to dark orange.

PEACH KERNEL OIL gives similar colors, but fainter and only after some time.

OLEUM AMYGDALÆ ESSENTIALE.

In America, Benzaldehyde is largely substituted for Oil of Bitter Almonds. Frequently Hydrocyanic Acid in sufficient quantity is added to meet the requirements of the trade or the U.S.P. Sp. Gr. should not be lower than 1.045 to 1.07 at 15° C.; *e.g.*, a sample gave gravity 1.075 containing 6.44% HCN. A pure oil requires 1 to 2 parts of 70% alcohol for solution. As to chlorinated compounds: It is possible to produce Benzaldehyde showing

absence of chlorine compounds. However, the presence of chlorine is strong indication of substitution.

U.S. X. requires Sp. Gr. 1.038 to 1.06 at 25° C. Nitrobenzene is tested for by adding 10 drops of the oil to 5 Cc. of alcohol, then adding zinc dust and 2 Cc. of acetic acid and boiling the mixture for 10 seconds. No odour of phenyl-iso-cyanide should develop after rendering strongly alkaline with Liquor Potassæ on addition of a few drops of Chloroform and heating. BENZALDEHYDE is assayed by means of Phenylhydrazine.

An oil adulterated with 2.5% Benzyl Benzoate has been recorded.—Y.B.P. /24,79.

BENZALDEHYDE.—Liable to spontaneous ignition if badly packed, *e.g.* in leaky tins surrounded with wood shavings, or on filter paper.—Y.B.P. 1922,54,55.

A British patent described its preparation by passing commercial Toluene and air over a catalyst at high temperatures (300—700° C.). A mixture of metallic oxides, *e.g.*, Copper, Molybdenum, Uranium, etc., is employed as catalyst.—P.R., '24,57.

AQUA LAUROCERASI

It has been held that the method of preparation in the FR. CX. is impracticable. The FR. CX. assumes a content of 0.12 to 0.16% HCN in the leaves. They never yield 0.10%. The previous FR. CX. formula was only $\frac{1}{2}$ this strength, viz., 0.05%. If the leaves are well crushed or disintegrated, not used entire or merely cut, the content of HCN in the water may be 1.5 to 1.7 per 1,000.

The bright green young *Prunus Laurocerasus* leaves were found to yield from two to four times the amount of Hydrocyanic Acid given by the older and more leathery brown leaves of cherry laurel. Adequate manuring causes increase in the amount of Hydrocyanic Acid contained.—D. H. Western P.J. i./04,643.

Test to distinguish Artificial Aqua Laurocerasi (made from Benzaldehyde, Hydrocyanic Acid and Water) from the genuine. Add a few drops of Congo Red solution to a few Cc. Bright red colour with the genuine, bluish or violet tint with artificial; Benzaldehyde owing to trace of Benzoic Acid acts on the Congo Red like an acid.—P.J. ii./10,438.

AMYL ALCOHOL 'A.R.'

Tests.—10 Cc. should leave no residue on evaporation.

For Furfural:—Not more than a pale yellow or reddish brown should be produced on shaking with equal volume of Sulphuric Acid.

Miscibility:—10 Cc. should mix completely with 10 Cc. of Hydrochloric Acid, Sp. Gr. 1.17; the addition of 1.5 Cc. of water should produce a permanent turbidity.

Oily Impurity:—2 Cc. with 10 Cc. of water and 10 Cc. of Sulphuric Acid should not show any oily layer after centrifugalising in a graduated Gerber milk tube several minutes.

AMYL NITRIS.

Tested by means of Allen's Nitrometer, a 5% solution in alcohol should yield not less than 7.9 times its volume of nitric oxide B.P. '14.

Our experiments show that this Standard is readily attainable, but it is important to observe that the yield of gas will vary from one experiment to another whilst using samples from the same (freshly made) Alcoholic Solution. This we believe, is due to slight differences of working—the amount of shaking in the nitrometer, etc. Actual figures, for example, in one set of experiments were 7, 7.3, 7.6, 8, 8.2 and 8.5. As the errors cannot be in the negative direction it is imperative to take highest readings when reporting upon a sample.

P. Jap. allows 0.6% acidity calculated as HNO₂, i.e., 5 Cc. shaken with 0.1 Cc. of Ammonia Solution 10% and 1 Cc. water—the water must not be less acid. Our examination of Amyl Nitrite by the test showed considerably less than this.

P.G.VI. Test (for free Acid) is similar to P. Jap. It must not become turbid on cooling to 0° C. (absence of water).

P. Helv. and P.G.VI. give test for Valerianic Aldehyde in.—1 Cc. warmed with 3 Cc. of a mixture of equal parts of Alcohol and Silver Nitrate and a few drops of Ammonia: must not blacken.

Amyl Nitrate. $C_5H_{11}NO_3=133.096$.

Colourless liquid, Sp. Gr. 0.999. Not used to any extent in medicine.

Amyl Acetate. *Syn.* ISO-AMYL ACETATE,— $C_5H_{11}.CH_3.COO=130.112$.

PEAR ESSENCE.—Made by action of glacial acetic acid on amylic alcohol in presence of a little sulphuric acid. Colourless Liquid. Miscible with alcohol and ether. Sp. Gr. 0.876. B.Pt. about $138^{\circ}C$. Is used to dissolve resins in varnish making and in preparation of Collodions.

Commercial Amyl Acetate contains some of the other isomerides. As 3 isomers of Amyl Alcohol exist the acetate will vary considerably in different preparations. The iso-amyl form is generally present in dominant amount.

ANTIMONIUM.

Sb = 121.77.

ANTIMONY IN PHARMACY AND CHEMISTRY. History and occurrence. Alloys for anti-friction surfaces—Babbitt's, Magnolia, etc. Also type-founding alloys. Antimony Tartrate of great value in schistosoma infection (*cf.* our Vol. I., p. 162).—G. M. Dyson, P.J. ii./28,397,520,596.

Antimony Poisoning from drinking lemonade (made with 'fruit crystals') prepared in glazed enamel buckets.—L. i./28,204,337.

Fur Dermatitis found to be due to presence of Antimony, 1 in 1000 of the fur (discovered by placing tadpoles in water with pieces of fur). Sweat promotes process of dissociation of the unstable aniline dye compounds with Antimony, and Sodium Chloride may provide the Antimony Chloride, giving rise to dermatitis.

Bandrowski's Base and similar Quinone bodies arise from the use of Para- and Meta-phenylenediamine and oxidation. Tartar Emetic is a well-known mordant.—J. Wilson Dougal, P.J. i./28,215.

Toxicology of Antimony. 1 of Antimony Tartrate in 50,000 might be tolerated by a tadpole, but 2 out of 2 tadpoles died in a 1 in 5000 solution in 34 hours. A solution of 1 in 1000 painted on the skin produced rash in 24 hours.—J. Wilson Dougal, P.J. i./28,215,225; C.D. i./28,354.

Determination of Antimony in fæces, etc.—The specimen is extracted with hot dilute Hydrochloric Acid, the filtrate saturated with H_2S and heated, the ppt. is collected, washed and dried, evaporated with fuming HNO_3 and weighed as Sb_2O_3 .

Antimony Ores. In the assay of crude Antimony it was observed that the Antimony slightly exceeded in amount that required by formula Sb_2S_3 . Deficiency of Sulphur probably owing to presence of Oxide.—P.J. i./13,337.

ANTIMONY AND BISMUTH DETECTION IN BIOLOGICAL LIQUIDS.

The reagent used is 1 Gm. Antipyrin, 2 Gm. of Potassium Iodide, in 30 Cc. of water. Biological fluids are evaporated and ignited, and the residue dissolved in Hydrochloric Acid and the reagent added; 0.025 mgm. Antimony can be detected, while Bismuth under similar conditions gives a brick-red precipitate.—J.C.S., A. ii./23,587.

Antimonii Chloridum, $SbCl_3=228.141$.

In colourless crystals. It is very corrosive and hygroscopic, hence **Butter of Antimony** used in veterinary practice is usually liquid; on addition to water, it decomposes into free hydrochloric acid and basic antimony oxychloride, powder of Algaroth; but is soluble in alcohol and carbon bisulphide. **Liquor Antimonii Chloridi.** B.P. 1885.

A caustic liquid of reddish colour (due to iron as impurity) Sp. Gr. 1.47.

Antimonium Sulphuratum (B.P.'14)

Estimation process. Oxidation with Sodium Peroxide, reduction and ultimate titration with Standard Iodine Solution. The antimony content should never be less than 30%.—P.J. ii./99,143.

ORGANIC ANTIMONY COMPOUNDS.

Antimony Analogue of Arsenbenzol. Prof. G. T. Morgan made a body giving data corresponding with the formula $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{Sb} = \text{Sb} \cdot \text{C}_6\text{H}_4 \cdot \text{NH}_2$ —the Antimony in this is in the same position as the Arsenic in Arsenbenzol. See also Von Heyden's D.R. Patents 259,875; 261,852.

p-Amino-phenyl-Stibinic Acid—the Sodium Salt of which is the Antimony Analogue of Atoxyl is patented.—Von Heyden, D.R.P., 254,421. J.S.C.A., i./13,416.

The analogue of Arsacetin is Stibenyl, see Vol. I., p. 168.

For further on Organic Antimony Compounds, see Vol. I., 19th Edn., p. 161, et seq., and Prof. G. T. Morgan's 'Organic Compounds of Arsenic and Antimony' (Longmans).

ARGENTUM.

Argentum Purum Præcipitatum.

Manufacture.—Dissolve Silver Nitrate 1 in Water 10 and add Sodium Carbonate 2 in Water 6 and Glucose 4, in Water 4. Boil gently (or the metal will become granular and will not powder) until the black precipitate at first formed turns light grey, then wash with boiling water and dry.

Uses.—Has been given internally in gastric ulcer and ulceration of the cæcum.—B.M.J. i./11,1313; ii./11,904.

Argentice Hair Dye (Black or Brown).

No. 1 Solution.—Silver Nitrate 1, Distilled Water to 12.

No. 2 Solution.—Sulphurated Potash 1, Distilled Water to 8. After washing and drying the hair, the solutions to be applied separately, in above order and after 2 minutes the hair well washed with soft water. This dyes brownish black with one application, but lighter shades may be obtained by using a weaker strength of No. 1 solution, which should not be allowed to touch the skin.

Pyrogallol Hair Dye (Black).

No. 1 Solution.—Pyrogallic Acid 1, Alcohol (90%) 8, Distilled Water 40. Apply before No. 2.

No. 2 Solution.—Silver Nitrate 1, Strong Solution of Ammonia 1, Distilled Water to 8. Use as last.

This dyes grey hair *jet black* with one application.

Various other formulæ for "Silver Hair Dyes"—modifications of the above, e.g., using a small addition of Sodium Meta-bisulphite in the No. 1 solution have been tried producing analogous result, but the difficulty about these preparations is that they simultaneously stain the skin.

Copper Pyro Hair Dyes (Odourless).

LIGHT BROWN.—Cupric Chloride ($\text{CuCl}_2 + 2\text{H}_2\text{O}$) and Pyrogallol of each 1 Water 100.

DARK BROWN.—Cupric Chloride 1, Ferric Chloride 0.5, Pyrogallol 1.5, Water 100.

BLACK.—Cupric Chloride 0.6, Ferric Chloride 2, Pyrogallol 2, Water 100. This produces a fairly natural tint.

Iron Tannate Hair Dye. Stated to be non-injurious (*black*). After washing the hair and drying it, brush the following thoroughly into the hair: Ferrous Sulphate 0.6, Glycerin 32, Water to 500. Repeat the process each day for 3 days. Then with a fine comb apply Gallic Acid 0.25, Tannic Acid 0.25, Water to 50.—Jl. A.M.A., per P.J. i./26,5.

Amidol Hair Dye (Black). Amidol 80 grains, Sodium Sulphite 120 grains, Alcohol 10%, 1 ounce.

This formula we found the best *black dye that will not stain the skin*. The colour develops gradually, the excess of the solution dabbed on can be slightly washed out, leaving the hair dark brown, but to produce a black several applications may be needed. We found that grey hair so dyed will stand vigorous washing with soap and water without appreciably affecting the colour. It did not appear to rot the hair. The hair should be free from grease. The solution deposits the colouring on the side of the bottle. It is odorless and a *one solution dye*.

The chemistry of hair dyes.—H. S. Redgrove, C.D. ii./28,760.

ARSENICUM.

The history of Arsenic.—B.M.J. i./24,1149.

Arsenic Eating.—20 grains of coarse powdered arsenic consumed daily in an arsenic factory. Wishing to give it up, the man promptly had severe gastric pain and diarrhoea, collapsed and died.—B.M.J. ii./09,1803.

Poisoning in China from eating a large piece of native Arsenic. Recovery under lavage with diluted Condy's Fluid, but subsequently evacuations were almost all dark blood. Hæmorrhage into the intestinal canal about region of the duodenum diagnosed. Death.—L. ii./10,1138.

Toleration of Arsenic. Gradual increase in dose to $1\frac{1}{2}$ grain.—L. i./14,236.

Arsenious Oxide in Neutral and alkaline solutions.—W. H. Millar, P.J. i./28,214; C.D. i./28,352.

Hammond's Vermin Remedy contains a large proportion of Arsenic.

Arsenical Fly-papers, All (Sale of):

N.B.—**Poisons** by Order in Council, Feb. 26, 1925. *The Poisons Schedule now specifies 'Arsenic and all Preparations as while previously the instructions were Arsenic and its Medicinal preparations.'*

For previous conditions of sale and the Seddon case, see Vol. I. Edn. XVII.

Arsenic in Carpets. Poisoning by, in Germany.

Though the use of Arsenic as a carpet dye in Germany is illegal, poisoning from it is not rare. Patients complained of chronic diarrhoea, which ceased on leaving their homes, to recur on returning. The Arsenic probably reached the system by inhalation. In two women who suffered from anorexia, lassitude and tendency to diarrhoea, the blood counts are stated to have been typical of pernicious anæmia.—B.M.J. ii./12,1570.

Arsenical Poisoning from Apples, it is said, has occurred in consequence of incrustations from fruit sprays, e.g., Bordeaux Mixture and Paris Green.

Of 39 samples of Jonathan, King David and Newtown apples only five were found free from Arsenic, and eleven contained more than the statutory limit, and it was found in the flesh of the fruit to the extent of about 3 % of that on the peel. Even scrubbing was found to leave appreciable amounts of Arsenic on the fruit.—B.M.J. i./26,297.

Examination of 43 samples of Canadian apples for Arsenic showed one-sixth contained less than 1/10,000 grain per lb., and one-third contained 1/10,000 to 1/190 grain per lb. It would be necessary to eat 3 lbs. of raw apples at a time to ingest the minimal medicinal dose of Arsenic.—L. ii./26,81. *See also Analyst '26,132,291.*

Arsenic in Cocoa 1/40th grain per lb.—traced to Potassium Carbonate used to render the cocoa soluble.—B.M.J. ii./22,1273.

Arsenic in shell-fish.—L. ii./26,1229.

Industrial Arsenical Preparations (Dangers from the use of). The Poisons and Pharmacy Act 1908 removed many restrictions with regard to the sale of arsenical preparations. As a result of increased facilities of sale, the public has been exposed to increased dangers. Liquid weed killers are often strong solutions of Sodium Arsenite, and may contain 14% to 40% Arsenious Oxide. This is usually coloured, but there is apparently no legal requirement to colour the liquid preparations.

Arsenical Wood Preservatives contain Sodium Arsenite, not coloured. Lead Arsenate is used much for fruit-tree spraying, as is also Calcium Arsenite. Paris Green, *Syn.* Schweinfurth Green, Emerald Green, Mitis Green or French Green, i.e., Copper Aceto-arsenite, is also used. The sale of arsenical preparations should be limited to registered pharmacists and to persons who obtain a licence for the possession of same.—Sir W. H. Willcox, B.M.J. ii./22,371.

The solid form of weed killer is commonly a fine powder, usually coloured, e.g. the 'Eureka' Weed Killer mentioned in the Greenwood case. A sample was found to contain 60% Arsenious Oxide colored with Phenolphthalein. Accidental poisoning due to liquid weed killer occurred in Sussex in 1919, when a sack of sugar absorbed a quantity of liquid weed killer from a leaking tin placed beside it in transit in a rail carriage. In May, 1921, an inquest was held on a woman named Hanktelow at Beckenham. The source of the Arsenic appeared to be 'Eureka' Weed Killer. The action of Arsenic is that of a protoplasmic poison. An account of 180 grains of White Arsenic (see B.M.J. Feb. 5th, 1921) taken in mistake for Magnesia. Patient recovered

from immediate acute symptoms but died from severe multiple neuritis 3½ months later. 2 grains is usually accepted as a possible fatal dose. Death usually occurs within three days.

Arsenic in any shape or form in agriculture and horticulture is uncalled for. For surface-feeding weeds a 5% solution of Washing Soda in soapy water is quite as destructive as any Arsenical weed killer. In the matter of sheep dipped in Arsenical bath, the layer next the skin was found quite *dry*, whereas with a Sulphur dip the Sulphur particles were deposited on the skin.

—A. McCutcheon, P.J. i./26,109.

Monophenyldichlorarsine, *Syn.* "**Lewisite**," a slow-poisoning gas in the form of a thick brownish liquid, absolutely odorless and not lachrymal. Inhalation causes death either from burned lungs or pneumonia. While conducting experiments at the Imperial College of Science and Technology, S. Kensington, as to the value of the gas as an insecticide, Prof. H. Maxwell-Lefroy was almost overpowered by the fumes before he was aware of it—he thought he was safe because it had no ill effect on the flies with which he was experimenting. "If it were dropped on London, people would walk about while it was actually being inhaled and be unaware of it."—*Evening News*, March 31st, 1925.

When Arsenic is injected *intravenously*, only about 40% of the Arsenic administered is excreted by the fæces and urine by dogs and rabbits, and of this the major portion is introduced to the fæces by the bile. A large amount migrates to the lungs, suggesting an expiratory channel of excretion.

—F. M. R. Bulmer, Jl. Ph. and Exp. Ther., Vol. XXI. '23,301.

An inquiry of the Swedish Commission into chronic arsenical poisoning showed that normal urine might contain quantities of Arsenic hitherto associated only with chronic arsenical poisoning. The amounts present in the urine of persons on known diets varied from 0.0 up to 0.58 mg. per litre. Increase in secretion of Arsenic traceable to eating of fish (especially plaice) which might contain upwards of 3 parts per million, the Arsenic appearing in the urine within 24 hours.—B.M.J. ii./24,932.

Detection of Arsenic in Drugs.—The Pharmacopœia Committee of the General Medical Council recommended the following method:—

A solution of 4 Gm. of the drug is to be prepared as described in a series of special notes, and is to be diluted with water to a volume of 25 Cc. This solution is to be placed in a test tube of about three-quarters of an inch (about 2 Cm.) in diameter and 7 inches to 8 inches (18 to 20 Cm.) in length. Fragments of **granulated zinc** are to be put into the test tube until they reach to about two-thirds of the height of the liquid. Immediately after adding the zinc a small plug of cotton-wool is to be placed in the test tube above the liquid, and then a plug of **plumbised cotton-wool** so as to leave a short space between the two plugs, and a closely fitting cap formed of two mercurialised test papers to be fastened on; it must not be torn at all when fastened on the test tube. The test is to be allowed to continue for two hours at least, and the test paper is to be examined by daylight for a yellow stain. The test should be conducted in a place protected from strong light. It is applicable both in the case of arsenious and arsenic compounds.

Limit of Arsenical Contamination.—3 parts per million is an adequate limit for drugs given in small doses. It is equivalent to $\frac{3}{160}$ grain white arsenic per pound. $\frac{1}{160}$ grain of arsenious oxide per pound, *i.e.*, 1.08% of arsenium per million, is a reasonable limit for tartaric and citric acids, which are largely used in foods and drinks, *cf.* also **Acidum Tartaricum**.

Bettendorf's Reagent for arsenic is a concentrated solution of stannous chloride in hydrochloric acid. A colorless arsenical solution will deposit brown metallic arsenic in the cold or on warming.

Gutzeit's Test. The substance to be examined is placed in a test tube with some arsenic-free zinc and sulphuric acid. The tube is plugged with cotton wool, and covered with filter paper having a spot of silver nitrate solution. A yellowish stain resulting in a few minutes indicates presence of arsenic. A control with lead acetate paper should be conducted to obviate confusion with sulphur.

A modification of the test consists in employing alkali instead of acid for generating the hydrogen and using a spot of mercuric chloride as in the customary test for arsenic in glycerin.

Modified Apparatus for Gutzeit's Test.—A four ounce wide mouth bottle is fitted with I.R. cork and a glass tube 200 mm. long and internal diameter

5 mm., open at both ends, the lower end drawn out with small hole about 1 cm. from end at constriction. This arrangement allows condensed water to drip back into bottle while providing free upward passage for the gas. Roll of lead paper 10 Cm. long prepared with 10% solution of lead acetate and subsequently dried and pushed into tube so that upper end is 2 cm. from top of tube. Cap of mercuric chloride soaked filter paper (5.5 cm. in diam.) fits over top in ordinary manner. The hydrochloric acid used should contain a small percentage of stannous chloride to assist in gas evolution and to reduce arsenic to the "ous" state. Also to make results comparable with the standard, which is arsenious anhydride in hydrochloric solution, strength 1 Cc. = 0.00001 Gm. Stannous chloride is made by diluting the B.P. (1898) solution with equal volume of hydrochloric acid and boiling to eliminate arsenic completely. Filter and make up to original strength. One per cent. of this is added to the strong hydrochloric acid employed in the tests. Use 10 Cc. of the acid (containing 1% stannous chloride solution), 50 Cc. water and 10 Gm. zinc. $\frac{1}{500}$ th milligram of arsenium calculated as arsenious oxide gives distinct yellow stain, *i.e.*, one part in 5,000,000 can be detected and estimated. In the estimation of iron compounds distil the arsenious chloride after reducing to the "ous" condition. After dissolving, *i.e.*, in hydrochloric acid and potassium chlorate, add stannous chloride drop by drop to reduce completely, as seen by the yellow colour of the solution being discharged.—C. A. Hill and J. C. Umney.

The modified Gutzeit Test is used in the B.P.'14 with precise directions and a list of Limits of Arsenic in the substances to be tested is given in parts per million.

Marsh's Test consists in generating hydrogen by means of pure acid and zinc, and to these is added the substance to be tested. If arsenic be present arseniuretted hydrogen is evolved, which deposits metallic arsenic in the cooler parts of the delivery tube, which is heated at a suitable point by aid of a Bunsen burner.

The deposit may also be allowed to form on a cool porcelain dish and is soluble in Chlorinated Lime Solution.

The addition of a little copper sulphate gave a mirror with only 0.0001 mgr. of arsenic, whereas platonic chloride (the customary addition to activate) only showed presence with 0.001 mgr.—P.J. ii./o6,325.

The **Sensitiveness of Zinc** is invariably increased by the use of **Cadmium Sulphate** and the use of this salt must be regarded as an essential and inseparable feature of the Marsh-Berzelius process.

To test Cadmium Sulphate for Arsenic, 10 Gm. should be distilled with Arsenic-free Hydrochloric Acid (20 to 30% HCl.) and 0.05 Gm. of pure Ferrous Chloride. The distillate measuring 20 Cc. when introduced into the Marsh-Berzelius flask, should not give an arsenic mirror after 30 minutes.—'A.R.'—See J.L.S.C.I., 1902, 21, 94, Analyst, 1902, 27, 45, and 1907, 32, 247, and 1906, 31, 3.

The Marsh-Berzelius Test best. It will show 1/1000 mgr. or about 1/70,000 grain.—A. J. Jones, P.J. i./22, 194.

Estimation of Arsenic specially with regard to determination in the tissues. Zinc is unsatisfactory. We entirely agree with the author that the Arsenic, *e.g.*, in a Marsh, does not appear until the experiment has proceeded for a period of time. The suggestion that there may be deposits or nuclei of Arsenic in impure Zinc is certainly good. The **electrolytic apparatus of Thorpe** is preferable to Marsh.—G. Roche Lynch, L. ii./22, 629.

Reinsch's Test consists in introducing copper to a hydrochloric solution. Cuprous chloride and hydrogen are formed. The latter reduces the arsenic to hydride: this reacts with the cuprous chloride, giving hydrochloric acid and depositing copper arsenide on the strip of metal employed.

For **QUALITATIVE EXAMINATION** in organs of the body the Reinsch Test is best.

For **QUANTITATIVE EXAMINATION**—if the amount is weighable, convert the Arsenic into Sulphide and check purity by conversion in Magnesium Pyroarsenate. Where not weighable, the electrolytic Marsh-Berzelius Test is best.—Sir W. H. Wilcox, B.M.J. ii./22, 118.

Sodium Arsenate.—Comparison of various methods of estimation.—J. E. Corfield and Elsie Woodward, P.J. i./21, 473.

Electrolytic determination of Arsenic in chemicals.—N. Evers, P.J. i./26, 183.

[P1] ORGANIC ARSENIC COMPOUNDS.

Tests to distinguish Organic Arsenic Bodies.

A solution of Arrhenal (strongly acidified) gives, with H_2S , a precipitate of mono- and di-sulphide of Methylarsine. Solutions do not precipitate with Baryta Water (Sodium Cacodylate does), neither with Magnesia mixture (nor does Sodium Cacodylate), nor by cold solution of Calcium Chloride (ditto Sodium Cacodylate), but are precipitated by nitrates of Silver (white silky ppt.; Sodium Cacodylate none), and Mercury (also Sodium Cacodylate; both yellow, Arrhenal the darker of the two). Mercuric Chloride gives a reddish-yellow ppt., with Arrhenal and a white precipitate with Sodium Cacodylate.

Sodium-p-aminophenylarsonate gives a white precipitate with these reagents in every case.

See also *Tests for Arsenobenzol Recognition in Medico-Legal Cases. p. 43.*

[P1] Sodii p-Aminophenylarsonas. Syn. ARSAMIN (cf. Vol. I.).

Poisonous Effects.

Action of Atoxyl on the eye. Records of 95 cases of disturbance of vision. The ocular symptoms comprise a more or less marked diminution of sight power and the field of vision is concentrically diminished, but more on the nasal than on the temporal side. Ophthalmoscopic examination at first gave negative result save that the retinal arteries may be narrowed, the veins somewhat hyperaemic—later there is complete optic atrophy, with increased dimness of vision going to complete blindness. Alcoholism may predispose to Atoxyl amblyopia. Arsacetin, though less toxic, is less active therapeutically.—L. ii./10,1149.

Arylarsonate Poisoning Treatment.

Large quantities of water (90 to 100 ounces) daily as well as electricity to the temples sufficiently strong to produce subjective flashes of light. For ten weeks daily for 4 to 6 minutes constant current of 3 to 10 milliamps, with an electrode on each temple. Vision steadily improved.—B.M.J. ii./10,623 (cf. B.M.J. i./10,724 & 725).

To test the purity of Sodium Arsanilate.

Apart from estimation of arsenic content and determination of water of crystallisation, it may be mentioned that precipitation with Silver Nitrate is of little use to indicate arsenate as impurity. From our experiments it will not show more than 0.5% by color of the precipitate.

Sodium Arsanilate is reduced in the Marsh apparatus, yielding the usual black stain on porcelain.

To detect Arsenate as impurity in Sodium Arsanilate we found it is best to dissolve 0.5 Gm. in 2 Cc. Hypophosphorous Acid, warming and diluting to 10 Cc. with water, than add 5 drops of Hydrochloric Acid, pass H_2S through the liquid, and warm slightly alternately. A bright orange yellow pp. will form rapidly if 0.1% Sodium Arsenate be present as impurity (W.H.M.). The Sodium Arsanilate in this method is not decomposed by the Sulphuretted Hydrogen.

[P1] Hydrargyri Arsanilas. MERCURY ATOXYLATE (MERCURY p-AMINO-PHENYLARSONATE). Syn. ASYPHIL. $(NH_2-C_6H_4.AsO.OH.O)_2Hg$.

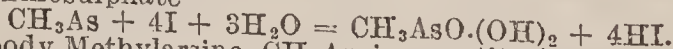
A white powder slightly soluble in water; was tried in syphilis.

Aromatic Arsenic Compounds for chemotherapeutic research. A general review.—Jacobs & Heidelberger, J.C.S.A. i/20,107 *et seq.*

ESTIMATION OF ARSENIC IN ORGANIC SUBSTANCES.

Several methods are provided in a paper by the author on "Organic Arsenic Compounds," Int. Cong., 1909.

Arrhenal may be estimated by dissolving about 0.2 Gm. in 1 to 2 Cc. of water and adding 15 to 20 Cc. of a special Hydrochloric and Hypophosphorous Acid test (*v. infra*). After twelve hours, dilute with 20 Cc. of water and filter, washing the residue with water. To the filter and its contents add a known excess of N/10 Iodine solution, shake well, and titrate the excess with Sodium Thiosulphate—



The black body Methylarsine, CH_3As , is quantitatively produced from one molecule $CH_3AsO.(ONa)_2$, therefore 4 atoms of Iodine = 1 molecule Arrhenal.

To prepare the test dissolve Sodium Hypophosphite, 20 Gm., in 20 Cc. water and add 200 Cc. Hydrochloric Acid (1.17 sp. gr.). Sodium Chloride is thrown out and removed. To apply the test for detecting traces of Arsenic

in Glycerin (Arsenite or Arsenate) 5 Cc. Glycerin are mixed with 10 Cc. of the reagent. Place in water-bath—brown deposit.

Methylarsine CH_3As is also obtainable by action of Sodium Hypophosphite and Sulphuric Acid on Sodium Cacodylate, $2\text{H}_3\text{PO}_2 + \text{AsCH}_3\text{O}(\text{OH})_2 = 2\text{H}_3\text{PO}_3 + \text{CH}_3\text{As} + \text{H}_2\text{O}$, as a yellow oil insoluble in water, with strong garlic odour. It polymerises to $(\text{CH}_3\text{As})_n$.

The following is simple (arranged by the author), and gives good results : Powder the substance carefully, mixing with about equal quantity of potassium nitrate, moistening with water, then oxidise with nitric acid, taking up the dried material with acetic acid, adding sodium acetate solution, and titrating with Standard Uranium Acetate Solution 1 Cc. = 0.0053 gram arsenium. For example 0.464 gram Arsenium required 20.2 Cc. uranium solution = 0.10706 gram arsenium = 23.08 per cent. (theory with $4\frac{1}{2}\text{H}_2\text{O}$ = 23.4 per cent.).

P.G. VI. gives the following for the acetylated body (*Arsacetin*) :—

Dissolve 0.2 Gm. in a stoppered flask in 10 Cc. of Sulphuric Acid, using slight warmth. 1 Gm. of powdered Potassium Permanganate is added carefully in small portions, with shaking. When reaction subsides dilute well with 30 Cc. of water and add 1 Gm. of Oxalic Acid. The clear and colourless liquid is now diluted with a further 30 Cc. of water and after adding 2 Gm. of Potassium Iodide is titrated after $\frac{1}{2}$ hour with N/10 Sodium Thiosulphite without addition of an indicator. 0.2 Gm. should require 11.3 to 11.6 Cc. of N/10 'Thio,' representing 21.2 to 21.7% As. (1 Cc. of N/10 'Thio' = 0.003748 Gm. As.).

The process given by H. A. Ewins, namely, treating with potassium sulphate and sulphuric acid, with the addition of a little starch, heating until clear and almost colorless, then alkalisng with 50% Potash, cooling, re-acidifying, adding excess of Sodium Bicarbonate and titrating with N/20 Iodine (C.D. Nov. 25/16) we have also tried—the results being practically identical with those by the author's method.

A mixture of the substance (0.2 Gm.), 20 Cc. water and 4–5 Gm. of Ammonium Persulphate is heated to brisk ebullition in a 300 Cc. flask. When colourless, 40 Cc. of N/1 Oxalic Acid are added, and the mixture further heated for 2 minutes after noticeable evolution of Carbon Dioxide has ceased. 2 N/1 Sulphuric Acid (20 Cc.) and 10 Cc. 10% Potassium Iodide solution are added, together with fragment of porous pot. The mixture is once more boiled until liberated Iodine is almost completely expelled. The remaining pale straw colour is discharged by N/20 Thiosulphate, the solution diluted to 100 Cc., 30 Cc. 2 N/1 Na_2CO_3 added, and the mixture treated with NaHCO_3 , about 1 Gm. in excess of that required to neutralise to litmus. After warming to 35–40°, the solution is titrated with n/10 Iodine, using Starch.—G. Newbery, J.C.S.T., '25, 1751.

To conduct the **Marsh Test** on Salvarsan oxidise with either Nitric Acid or with Potassium Chlorate and Hydrochloric Acid. The solution thus obtained is then reduced with Potassium Meta-bisulphite and dilute Sulphuric Acid and the excess of Sulphur Dioxide boiled off. This solution contains the arsenic in form of Arsenious Acid and is suitable for use. For further details on Toxicology see Sir W. H. Willcox, B.M.J. 1./16, 474.

P1 Arsenobenzol.

Introduction.—

Ehrlich's first Salvarsan he called No. 606 in 1910, but information as to how long he worked on these preparations up to that date is not forthcoming. In 1913 he brought the number up to 1206A (Salvarsan Sodium, *q.v.*), that is another 600. Reckoning this period (from 1910 to 1913) as 900 days, this means a new preparation built up, examined pharmacologically and tested clinically every $\frac{2}{3}$ of a day. The statement is staggering to anyone who has worked in a laboratory, and almost unbelievable.—Gordon Sharp, P.J.ii./15, 756.

Salvarsan was first tried (by Hata) on a human case at the Imperial Institute at Tokyo. For details of the earlier work, see *Edn. XVIII., Vol. II., p. 37.*

A few phrases occur in the literature :—

Chemotherapy.—"The principle of this is to employ chemical substances in infectious diseases in which the natural recuperative powers of the system assisted by the formation of specific antibodies, are unable to bring about a restoration to health. All the early preparations acted destructively on the

antibodies, but the new substance was found in its action on spirillosis in animals to hinder the development of parasites whilst not being harmful to the patient, at least in the doses required to destroy the parasites."

Parasitotropic Chemicals possess a strong avidity for the parasites and will kill them in the living being without injuring the tissues or organs in contradistinction to *organotropic* substances.

Ehrlich, in his division of chemical bodies, points out that all substances which are parasitotropic are *also poisons to the living organism, i.e.,* are also organotropic. Practically, therefore, one can only use as curative bodies those in which the *organo and parasitotropic properties* are in the right proportion.

Organic Arsenic compounds **owe their action to their organotropic properties** rather than to a direct action on parasites such as the spirochaetes of syphilis or trypanosomes. **Chemotherapy** has lost its original significance and **has come to mean specific treatment.**
—Dixon.

Therapia Sterilisans Magna was a phrase used by Ehrlich to denote the rapid killing off of all the specific germs by introducing a sufficiency of a parasitotropic chemical.

Unfortunately this *Therapia sterilisans*, except in rare instances, has not proved capable of realisation. It is exceptional that a single dose of Arsenobenzol cures an attack of syphilis, in fact, three or four injections may not cure; but it is the most powerful weapon we have against spirochetes.

According to one authority, if the preparation is rendered very slightly alkaline—almost neutral—the solubility is at its minimum; this amount of alkalinity corresponds very closely with that of the blood and tissues. Probably the *relatively low toxicity in comparison with other Arsenic preparations is due to the fact that it is so insoluble in the blood.* This authority thinks that no matter in what form the substance is introduced the solubility is never more than 1/1000 per cent. The concentration in the blood, therefore, can never exceed this slight amount.

Attention may also be drawn to the "parasitotropic" importance of the unsaturated **trivalent Arsenic**—as is seen in the structural formula (compare, e.g., the Asv in *p*-oxy-phenyl-arsonic Acid or in "Atoxyl," "Arsacetin," the Cacodyl compounds, etc.). The fact of the OH being in the *para* position to the Arsenium in the formula is also of importance.

An immunity to syphilis does not exist, neither immunisation nor serum-therapy are possible; hence the value of the new 'chemo-therapy.' Syphilitic infection, according to Neisser, takes place throughout the entire system very rapidly after it is created—indeed, there is probably a saturation of the system through the blood stream at the moment of infection.

Tests.—Animal Experiments.

The following procedure is adopted in the MED. RES. COUNCIL'S REPT. OF BIOLOGICAL STANDARDS.

Tests for Toxicity.—

(a) '606.' The preparation, in 1% alkaline solution injected intravenously must be tolerated by mice in a dose of 0.1 milligram per gram of body weight.

The period of observation is 3 days, and, out of 5 mice injected with this dose, 4 or 5 must survive without serious symptoms, if the preparation is to be passed without further test. If 2 mice out of the 5 die in the prescribed period, the sample is retested on a higher dose, namely, 0.125 mgr. per gram, and, if 4 mice out of 5 should survive on this higher dose, the preparation is passed as not unduly toxic. If more than 2 mice die, out of 5, with 0.1 mgr. per gram, the preparation is at once rejected.

(b) '914.' The preparation is injected in 6% watery solution intravenously into mice—the standard dose being 0.3 milligram per gram.

The period of observation is one week. If not more than 1 mouse, out of 5 injected with this dose, fails to survive, the preparation is passed forthwith, unless severe symptoms follow the injection. If 2 mice out of the 5 die, and the others show no serious symptoms, the preparation is retested on a dose of 0.4 milligram per gram, and passed if not more than one mouse out of 5 dies. If more than 2 mice out of 5 die on the standard dose, or, in any case, if the mice, though surviving, show serious symptoms of intoxication after the injection, the preparation is rejected as unduly toxic.

A Modification of the Test is suggested in Reports on Biological Standards (M.R.C. Spec. Rept. Series, No. 128, 1929), Toxicity Tests for Novarsenobenzene, by Durham, Gaddum and Marchal. This is a 40-page book

with elaborate tables dealing with, *inter alia*, the variability of mice used and comparison of standards of other countries. The new method advised is as follows:—

(1) 10 mice each 18–20 Gm. are each injected with 7·6 mgr. in 2% solution. If not more than 20% die the sample is satisfactory.

(2) When more than 20% mortality occurs, the same dose is injected into another 10 mice. If these 20 injections have not produced a 40% mortality then the sample is passed. Similarly a sample which has killed 15 out of the 20 mice can be rejected without further test.

(3) When more than 8 but less than 15 mice have been killed a further 10 are injected. Then samples which have killed more than 15 out of the total of 30 are rejected and the remainder passed.

Therapeutic Tests.

These are carried out on mice infected with *Trypanosoma equiperdum*. The mice are injected with diluted blood from a heavily infected rat, and the mice chosen for the test must show an infection, in blood taken from the tail vein, of the order of 100,000 to 500,000 trypanosomes per cubic millimetre.

The preparations are administered by intravenous injection—‘606’ being given in 0·1% alkaline solution, ‘914’ in 0·2% solution in physiological saline.

5 mice are injected with the standard dose, and all must be free of visible infection in 48 hours, if the preparation is to pass as of adequate potency. The standard doses are, for ‘606,’ 0·009 milligram per gram, for ‘914,’ 0·03 mgr. per gram.

This therapeutic test is carried out as a routine on all samples of ‘914’ submitted for test, but it has not hitherto been found necessary to apply it regularly in the case of ‘606,’ which, being a substance of more regular composition, has not been observed to show material variations in therapeutic potency with different makes, or with different samples of the same make.

The main trypanocidal activity of active Arsinic Acids is due to their reduction to the corresponding oxides by the tissues, and acids, which are excreted by the system too readily owing to their great aqueous solubility, fail to exert the persistent and continuous action emphasised in the cases of Bayer 205 and its analogues. Out of over 2 dozen compounds of Arsinic Acid described only two proved to possess any therapeutic activity, and that only trivial.—G. A. C. Gough and H. King, J.C.S., Sept., ’28, 2431.

A small group of the trivalent Arsenicals, comprising Salvarsan, Sulpharsenol, Metarsenobillon and Kharsulphan, have **properties distinguishing them from almost every other compound used for the chemotherapy of bacterial infections.** The bactericidal action is most marked on hæmolytic-streptococci and pneumococci.

Streptococci of the *viridans* group and staphylococci are less affected, and there is hardly any action on enterococci and certain diphtheroid and coliform bacilli. The toxicity of Arsenic compounds for human leucocytes is in ascending order, as follows:—Metarsenobillon, Kharsulphan, Sulpharsenol (nearly equal), Stabilarsan, Salvarsan, Neosalvarsan, and Silver Salvarsan.—L. Colebrook, *Med. Res. Council Spec. Rept.*, Series No. 119, per P.J. ii./28, 251.

The League of Nations Commission on the standardisation of Serum, Serological Reactions and Biological Products decided to recognise a test for experimental action on animals infected with *Spirochætes*, as an alternative to that in which trypanosomes are used, and recommended that a 20% excess of toxicity above that of the standard would be a suitable limit for tolerance, and that the standard samples for Neosalvarsan and Sulpharsphenamine of Kolle and Voegtlin are suitable as regards toxicity and experimental therapeutic activity for adoption as the basis for International Standards.—B.M.J. ii./28, 111.

The absence of action of Salvarsan on spirochætes *in vitro* is ascribed to a solubility of the Arsenical in the “lipoproteins” of the micro-organism. *In vivo*, it is first converted to base, which possesses the necessary solubility, and, having penetrated the cell, it becomes attached through the amino groups to the acids of the lipoids, where its strong reducing action deprives the organism of Oxygen, and so kills it. The lower toxicity of quinquevalent Arsenic derivatives to spirochætes, as compared with trivalent derivatives, is stated to be due to the more acid nature of the former, and the consequent greater difficulty of converting them into bases soluble in the lipoproteins.—J. Schumacher, *Biochem.Z.*, ’25, 438, J.C.S.A., i./25, 733.

Chemical Characters.—A solution 1 in 10 should be clear and be neutral to Congo Red paper. If 5 Cc. of Solution (1 in 10) be precipitated with 4 Cc. of Sodium Acetate Solution by warming for a short period on the water-bath and then filtered, the filtrate acidified with Hydrochloric Acid, should not be affected by H_2S . Another portion of the filtrate mixed with 3 Cc. of Ammonia and 3 Cc. of Magnesia Mixture should not deposit or become turbid after long standing.

Ferric Chloride gives a deep blood-red colour not discharged by Concentrated Hydrochloric Acid. Bromine water gives a brown colour, becoming deep crimson in a few seconds.

We found that a 1% solution in an amber bottle decomposed in about 48 hours giving a deposit which re-dissolved in acid or alkali but gave no reaction for inorganic Arsenic. The supernatant liquor turns dark. There was no apparent change in 24 hours in the same sample, but in white glass test tubes there were signs of decomposition in less than 24 hours.

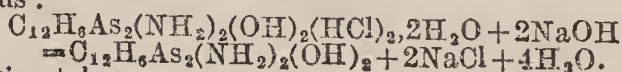
Arsenobenzol Dihydrochloride is, contrary to prevalent views, stable in the atmosphere. The addition of alkali, however, leads to a rapid increase in the rate of oxidation. The Sodium compound is first oxidised to the corresponding oxide and this simultaneously to the pentavalent Arsenical. NOV-ARSENOBENZOL is rapidly oxidised in the air. The nature and rate of oxidation of Arsenobenzol and Novarsenobenzol to the oxides provide an explanation of the increase in toxicity and trypanocidal activity when these solutions are exposed to the air.—C. Voegtlin & H. W. Smith, *Jl. Pharm. & Exp. Therap.*, Oct. 1920.

A colorimetric method for the estimation of Salvarsan, applicable to urine, blood, tissues, etc., depends on the diazotisation of the amino groups and coupling of the product with Orcin to produce a bright red substance.—Bull. Johns Hopkins Hosp., '23,34,149, per *J.C.S.A.* ii./23,800.

Salvarsan, commercial, derivatives of Sulphur in.—H. King, *J.C.S.*, 1921, 119,1107; *Y.B.P.* '22,155.

Chemistry of the Injections.

The reaction which takes place on bringing sodium hydrate, sufficient to neutralise, in contact with dioxy-diamino-arsenobenzol-hydrochloride may be indicated thus:



i.e. approximately:—

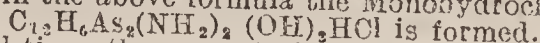
475.06 Gm. requires 2000 Cc. N/1 NaOH = 455.84 Cc. 15% w/w NaOH

0.4 " " 1.68 " " " = 0.38 " " " (6 minims.)

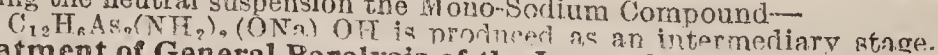
It is seen from these details that the **basic substance** is formed and is precipitated from solution.

This is the **Neutral 'Suspension'** as used in the *intramuscular injection*.

Using double the amount of alkali in each case will produce the soluble Disodium Compound $C_{12}H_6As_2(NH_2)_2(ONa)_2$ as employed *intravenously*. Clearly before the basic body is produced, by the use of half the amount of Sodium Hydrate in the above formula the Monohydrochloride



By the use of $1\frac{1}{2}$ times the amount of Sodium Hydrate in the directions for making the neutral suspension the Mono-Sodium Compound—



Treatment of General Paralysis of the Insane by Arsenobenzol alone, and combined with Human Serum. Antibody Formation Theory.

It is known that the milk of a syphilitic mother under treatment by Arsenobenzol cures the symptoms of syphilis in her infant. It was held from this that the cure has been effected by antibodies. The idea is, however, now discredited.

Salvarsan Serum gave improvement in a case.—*B.M.J.* i./11,585,809.

See also paper by H. Campbell and Sir Charles Ballance, *L.* i./19,608.

Untoward Results—Arsenic Retention—Deaths.

Arsenic retention is likely to occur by the intragluteal method of injection hence the intravenous method has been more advised.

Degenerative diseases of the liver due to Arsenobenzol treatment.—Sir H. Rolleston, *B.M.J.* ii./22,1055.

Experimental investigation into the cause of death from.—Jackson & Smith *Jl. Pharm. & Exp. Therap.*, Nov. 1918,221.

For further details see Vol. I., p. 201 and previous Edns. of Vol. II.

Jaundice during treatment. It is more common with 'Neo' than with the original.—R. Hallam, L. i./20,1356.

Delayed Arsenical poisoning from Arsenobenzol preparations. A report of 58 cases—8 fatal.—G. S. Strathey and co-workers, L. i./20,802.

According to McDonagh, Ehrlich's chemotherapy is not only the acme of speculation, but illogical from start to finish.—L. ii./16,121.

Deaths following Novarsenobillon injections. Toxic effect considered due to selective action of Arsenic on adrenals. Adrenalin 1 in 1,000 subcutaneously in 10 m. doses gave almost immediate relief and ultimate recovery in apparently almost hopeless case.—A. D. White and R. S. S. Chandra Dutt, I.M.G., Oct., '25, 465.

Impossible to predict what patient would prove unsuitable for Salvarsan treatment. Ill effects might occur at any time during the course with any brand of drug and with any sized dose.—W. J. O'Donovan, B.M.A. Ann. Meeting, B.M.J. ii./28,307.

Estimation of the Arsenic excreted in the urine has been conducted, the general *Conclusions* being (a) the elimination begins rapidly; (b) the duration of the passing of Arsenic in the urine is longer than was thought; (c) after *subcutaneous* injection the elimination is concluded more rapidly than in the intramuscular method; (d) simultaneous use of Mercury caused delay in eliminating the Arsenic; (e) Potassium Iodide given at same time shortens the duration of the Arsenic elimination.

It appears the excretion is much slower with Salvarsan than with Atoxyl or Arsacetin when injected subcutaneously; also that whilst Atoxyl and Arsacetin are excreted quickly and almost completely by the urine, in the case of "606" the Arsenic is largely to be found in the faeces.

After hypodermic, gastric or intramuscular use the elimination of Arsenic in the urine lasts about 25 days. The Arsenic, it is said, is largely changed into the ionic condition, and this may be related to its antisyphilitic action.—J.C.S.A. ii./12,968.

Tests for Arsenobenzol: Recognition in Medico-Legal Cases.

The behaviour of Salvarsan with the usual reagents for Arsenic has been investigated to find a method of distinguishing between it and inorganic arsenic in medico-legal cases.

Muscle from a patient who had died three weeks after injections of Salvarsan still gave reactions for Arsenic. The drug gives the Reinsch, Marsh, Gutzeit (after oxidising and reducing) and biological tests for Arsenic. The following serve to distinguish Salvarsan from inorganic forms of arsenic. With Bettendorf's reagent it gives an amorphous, yellow ppt. which dissolves on warming and reappears on cooling. H_2S gives no ppt. even after a solution of the drug has been boiled with HCl. The organic part of the Salvarsan molecule gives certain reactions, which may afford confirmatory evidence of the presence of the drug, thus:—the corresponding diazo-derivative gives a characteristic red to violet precipitate with α -naphthylamine, which may be isolated and examined for arsenic by Reinsch or Gutzeit test. Atoxyl behaves similarly, giving a red azo-dye, but the diazotised Salvarsan gives no colour with β -naphthylamine, whilst Atoxyl gives a vermilion-red azo-colouring matter with the β -amine.

Minced horseflesh sprayed with Salvarsan solution and kept for 14 days was extracted with Alcohol, slightly acidified with HCl. The residue so obtained gave positive results with the Reinsch, Gutzeit, and α -naphthylamine tests, but negative results with Bettendorf's reagent, and with hydrogen sulphide. So far it has proved impossible to obtain good results by applying to Salvarsan ordinary toxicological methods for the estimation of arsenic, the latter being obtained only to the extent of from 29 to 29.5% out of the 34% present.—J.C.S.A. ii./11,448. See also Sir W. H. Willcox, B.M.J. i/16, 474.

Wassermann's Reaction, Effect on.

The Wassermann Reaction is used to control Arsenobenzol treatment but opinions still differ as to its reliability. Accounts in the literature differ remarkably.

The reaction, according to some, cannot give a conclusive result with regard to success of the injection until after six or eight weeks.

Congenital syphilis tends to give + Wassermann throughout life and this is not altered, however much Mercury is given. *That* positive reaction should not be taken as indication that Salvarsan has no effect on the Wassermann's reaction in congenital syphilis. In *late acquired* syphilis on the other hand, Salvarsan may change the reaction.—McDonagh.—L. ii./10,1490.

Vagaries of Wassermann's Réaction before and after treatment.—H. C. French.—L. ii./12,228.

Salvarsan as a Test for Syphilis.—There is evidence that a spirochæte infection that has been in abeyance can be roused into sufficient activity to cause the Wassermann reaction to become positive, where previously (before injection) it had been negative. This result will enable the injection to be used as a test to say whether or not patient is cured of syphilis.—D'Arcy Power, B.M.J. ii./12,1606.

Blood Examination.—Blood examinations show leucocytosis after injection in some cases. May be as high as 30,000. Usual count is about 17,000 (McDonagh). See also *Pernicious Anæmia, Vol. I., p. 197.*

Examination for Spirochetes.—The spirochetes are stated to disappear from the blood in about 24 to 48 hours after injection, but it may take considerably longer, *e.g.*, up to 14 days.

McDonagh reviews the rationale of the action of Salvarsan and Neo-Salvarsan and concludes that a union takes place between the drug and the parasite with destruction of the latter. What the nature of the union is and why death of the parasite should follow are not explained. The action of the Arsenic according to McDonagh is merely catalytic—it is somewhat analogous with that of complement in the Wassermann reaction.

He says that Ehrlich's statement that Salvarsan is parasito-tropic only and not organo-tropic cannot hold good. For a drug to be parasito-tropic it must be organo-tropic. Its organo-tropic properties are indeed more important as most of the organisms are killed indirectly. The Salvarsan molecule becomes attached to the lipid globulin molecules of the serum which by a process of adsorption kills the parasites.—L. i./16,236,297. See also J. N. d'Esterre, L. ii./20,555.

¶1 * **Metarsenobillon** (T.M. 459,333).

The Disodium salt of 4:4 dioxo-3:3-diamino-arsenobenzene-diformaldehyde bisulphite. A yellow powder, containing approx. 20% of Arsenic, soluble, and giving a faintly acid solution.

USES.—By intramuscular or subcutaneous injection less painful than Novarsenobillon and giving greater effect than when injected intravenously. Stated to have low toxicity.

It is well adapted for use in the treatment of syphilitic expectant mothers and of congenital syphilis or infants and young children; also in neuro-syphilis.

DOSE.—0.1 Gm. gradually increasing to 0.6 Gm. as max. single dose. For infants 0.05 Gm. at weekly intervals. For children from 3-12, 0.2 Gm. For intramuscular or subcutaneous injection the dose is dissolved in 1 to 2 Cc. water. Concentrated solutions up to 30% can safely be used. Intravenously 2% solutions are employed (not recommended), but maximum efficiency obtained when injected intramuscularly.

The patient should fast for at least 3 hours before the injection and be kept in bed for several hours after. No solid food should be given for 12 hours following, but a little soup may be given after 4 or 5 hours.

Both the Triamino Acid and the Hexamino base are comparatively slightly toxic, and the latter has powerful spirilloccidal action.

1:3 Benzo-diazole Arsinic Acids and their reduction products have been prepared and studied by R. R. Baxter and R. G. Fargher, C.D., '19,1317.

W. H. Martindale communicated a paper on Organic Arsenic Compounds to the International Congress of Applied Chemistry, 1909, and introduced several compounds which at that time had not been used therapeutically.

Poly-amino-arsenobenzenes, notably **Hexamino-arsenobenzene** and **Triamino-phenylarsinic Acid** are further developments.

Trypanocidal action and chemical constitution of Arsenic compounds.—H. King, W. O. Murch and I. E. Balaban, J.C.S. /25,2632,2701.

Experiments on disappearance of trypanosomes from blood after injection of Monosodium salt of Tetra-arsenoacetic Acid, $\text{COOH} \cdot \text{CH}_2 \cdot \text{As} : \text{As} : \text{As} : \text{As} \cdot \text{CH}_2 \cdot \text{COO Na}$, are held to indicate that some therapeutic value attaches to the chain of 4 Arsenic atoms.—J.C.S. Ai./24,152, and Ai./25,733.

* **Flumerin** and **Mercuric Salicylate** are far inferior to Neoarsphenamine as healing and sterilising agents in experimental rabbit syphilis.—G. E. Wakerlin and S. Lœvenhart, Jl. Pharm. and Exp. Therap., Sept. /28,28.

Table of some Organic Arsenic Compounds showing Content of Arsenium (As), and Solubilities.

ARSENIC COMPOUND AND FORMULA.	Arsenium content per cent.	SOLUBILITIES.	
		Water.	Alcohol 90%
Acid. Cacodylic, $C(H_3)_2 AsO.OH$	54.23	2 in 1	1 in 4
Cacodyle, $(CH_3)_2 As-As(CH_3)_2$	71.4		
Cacodyle Oxide $(CH_3)_2 As_2O$	66.3		
Calcium Cacodylate $((CH_3)_2 AsO_2)_2Ca$..	47.7	2 in 1	1 in 2
Sodium Cacodylate $(CH_3)_2 AsO.ONa.3H_2O$	35.0	2 in 1	About 1 in 1
Magnesium Cacodylate $(CH_3)_2 AsO_2)_2Mg$	50.25	1 in 3	Insoluble
Iron Cacodylate $((CH_3)_2 AsO_2)_2 Fe$..	48.17	1 in 15	Insoluble
Gualacol Cacodylate, $(CH_3)_2 AsO.OH.C_6H_4.OH(OCH_3)$..	28.6	1 in 25	1 in 1.5
Strychnine Cacodylate $C_{21}H_{22}N_2O_2(CH_3)_2$ $AsO.OH$	15.8	hardly	1 in 80
Di-sodium Methylarsenate (Arrhenal) $CH_3AsO.(ONa)_5H_2O$	27.3	1 in 1	Slightly
<i>p</i> -Amino-phenyl-Arsonic Acid. $NH_2C_6H_4AsO(OH)_2$ (Arsanilic Acid) ..	34.5	Slightly	Slightly
Sodium-<i>p</i>-amino-phenyl Arsonate $NH_2C_6H_4.AsO.OH.ONa. + 4H_2O$..	24.09	1 in 6	1 in 125
Ditto Ditto Anhydrous	31.4		
Sodium Acetylarsanilate (Arsacetin) $C_6H_4NH.CO.CH_3.AsO_3HNa + 4H_2O$..	21.2 to 21.7	1 in 10	Insoluble
Sodium Acetyl Amino hydroxy-phenyl Arsonate (Stovarsol) $C_6H_3.OH.NH.COCH_3.AsO(OH)_2$ (as Sodium Salt)	27.21	Hardly in cold, slightly in warm.	Almost insoluble
Dioxy-diamino-arsenobenzol Di-hydrochloride. (Arsenobenzol) $C_{12}H_{12}O_2N_2As_2(HCl)_2.2H_2O$	31.56		
Novarsenobenzol $C_{13}H_{13}O_4N_2SAs_2Na$	—	Readily	Very slightly
Sodium Benzo-sulpho-<i>p</i>-amino-phenyl Arsonate (Hectine) $C_6H_5.SO_2.NH.C_6H_4.As.O.OH.ONa$..	19.77	Very soluble	Very soluble
Sulpharsenobenzene $(NaO.SO_2CH_2NH.OH.C_6H_3As)_2$	25.06	Readily	
Tryparsamide $H_2N.CO.CH_2.NH(C_6H_4As.ONa.O.OH)$..	25.31	Readily	
Silver Salvarsan P.G. VI.	22.5	Readily	

AURANTIUM.

Orange Flower Water is sold in many grades, and is sometimes found adulterated with the water obtained in distilling Petit-grain Oil ("Eau de Brouts"), and even with synthetic Neroli. The following modified Legal's Test is characteristic of the genuine product. To 10 Cc. of the sample add $\frac{1}{2}$ Cc. 10% Sodium Nitroprusside solution and 2.5 Cc. 5% Caustic Soda solution, and after 15 seconds $\frac{1}{2}$ Cc. Glacial Acetic Acid. An emerald green color is produced, and this changes to violet-red on the immediate addition of 2 Cc. 10% Zinc Sulphate solution.—P.R. '24,290.

Less appreciated constituents of Orange Juice.—S. G. Willimott, 1927 B.P. Conf., C.D. ii./27,33.

Terpeneless Oil of Orange (*cf.* also Essential Oils Table).

A note from Sicily says the process of manufacture is exactly similar to that for terpeneless Lemon Oil, *q.v.*, except that a larger quantity of Terpenes are distilled off—about 95%. No physical or chemical data are known for the finished product, as it is only very rarely distilled, and then it is not a great success. The odour of the Terpeneless Orange Oil does not pay for the distillation in many cases.—The Terpeneless Orange Oils on the market are usually "synthetic" products, *i.e.*, a mixture of which the chief odoriferous constituent is Methyl methylantranilate. The distillation in London and elsewhere is carried out more scientifically than in Southern Italy.

Neroli Oil (Artificial) is a mixture, the chief body of which is the methyl ester of Anthranilic Acid—to this the fragrance of the natural oil is due.

For genuine Neroli Oil, see Vol. I., p. 842.

Petitgrain.—This name is given to the young orange fruits which fall naturally after "setting." Oil of Petitgrain is distilled from them.

Petitgrain Oil.—Adulteration with Terpinyl Acetate. Detection by taking saponification value at 1 and 2 hours.—P.R., 1912,3,240.

Paraguay produces Oil of Petitgrain.—P.R., Dec., 1913, p. 414.

BELLADONNA.

Although Belladonna and Hyoscyamus owe their activity chiefly to the same alkaloid Hyoscyamine, their preparations are by no means interchangeable. Part of the difference of action may be due to the fact that **Hyoscyne** is present in larger proportion in Hyoscyamus than in Belladonna, thus accounting for greater sedative action.

Hyoscyamine if heated at 110° out of contact with air or allowed to remain in an alkaline alcoholic solution, is converted to atropine and the physiological activity is thereby modified. Atropine acts only half as strongly as Hyoscyamine on the peripheral nervous system, but it has an activity equal with that of Hyoscyamine on the central nervous system. Hence care is necessary in making preparations. The formation of Atropine is minimised by concentrating in vacuo. Without this precaution there is indeed risk of decomposing the Hyoscyamine altogether, forming tropine and atropic acid.—C. A. Hill, Pres. Add., B.P. Conf., 1920.

Assay and Alkaloidal Content.

Farr and Wright found a minimum of 0.14 and a maximum of 1.32% (exceptional) total alkaloids in the leaves, an average of 0.547%—rather more than is generally found in the root.

Roots of our own growing gave the following:—Second year's growth, 0.605%; fourth year's, 0.51%. Three years is believed to give about the best yield.

Third year roots attain good dimension with good alkaloidal content, and are suitable for use. J. J. Blackie found in Scottish-grown root, 1st year 0.72%, 2nd 0.65%, 3rd 0.66%, and 4th year 0.60%—agreeing with our findings.—P.J. i./26,231; C.D. i./26,307.

MacEwan and Forrester supplied figures indicating variability of the alkaloidal content—0.10 to 0.65%—the most frequent value being 0.451, and the mean 0.339%. Galenical preparations of Belladonna differ in action from the alkaloids contained. Alkaloid determination does not suffice. Thoms, it may be recalled, found in two Belladonna Extracts (P.G. earlier edition) each containing 1.72% alkaloids. 3.5 and 8.1% Tannin, 1.8% of other organic bases (in each); Permanganate numbers 81 and 256; and 15.7 and 11.5%

volatile matter,—showing that alkaloidal determination is not finality in evaluation. There is much divergence regarding pharmacopœial requirements, and analyses are necessary with the view of ascertaining if the drug is harvested at the proper season.

Experiments by A. F. Sievers at the Office of Drug Plant Investigation, Washington, on *Atropa Belladonna* (first, second, and third year's growths) showed that the alkaloidal content of the leaves of first year's plants (1910) gave an average of 0.547%, the highest being 0.7% and the lowest 0.334%; the same plants yielding approximately the same amount of alkaloid from season to season. The leaves can be picked to best advantage from the time of flowering until the early berries begin to ripen. Later the leaves are richer, but are too small and sparse for harvesting.—C.D. i./14,52.

Belladonna Leaf and Extract assay. With slight alteration in technique, the B.P. method is best.—C. M. Caines and N. Evers, B.P.C. 1926; P.J. ii./26,179; C.D. ii./26,237; P.J. ii./28,83.

Discrepancies in methods of assay of *Belladonna* and *Hyoscyamus* Leaves. Content of volatile bases in dry Henbane varies. The methods of the B.P. for leaves and preparations of leaves do not give comparable results. In the case of *Belladonna* Extract and the Tincture the residue is directed to be heated on the water-bath for $\frac{1}{2}$ -hour—there is no heating in the case of the leaves.—W. A. N. Markwell and L. J. Walker, C.D., Oct. 27/28.

Variation in alkaloidal content of *Solanaceæ*.—Y.B.P./26,39,40.

Pharmacological difference of the Solanaceous alkaloids.—B.C.A./28,A1155.

Brom-phenol-blue recommended as indicator for titration of Atropine. A solution of 1% Atropine Hydrochloride has P_H of 3.75.—N. Evers, B.P. Conf., 1921.

Colour reactions of Atropine and some related compounds.—B.C.A./28, A1145.

Assay of Atropine in Ointment B.P. '14. It is best to dissolve in Chloroform; extract with N/20 Sulphuric Acid and back titrate with N/20 KOH, using Brom-phenol Blue.—H. J. Foster, P.J. i./23,479.

Cultivation. *Belladonna* needs good drainage, warm hilly situation, and protection from direct sunlight.—E. M. Holmes, P.J. i./26,296. Cultivation in America.—Two crops of leaves are obtained—one at end of July and the second in October. If the roots are not required for use they should be taken up in October and buried in a shed to preserve from frost, to be divided into five or six rootlets in the spring for propagation. This procedure is better than growing from seed. An acre yields six to eight thousand pounds of herb.

The highest alkaloidal content was obtained from a plot which had not been manured at all, but which was **fully exposed to the sun**. This content (1.035% in the dry leaf) from leaf collected September, 1911, was the highest ever recorded as having been obtained. The content from leaves under similar conditions, September, 1910, was 0.44%, June, 1911, 0.65%,—each the highest as against plants grown with artificial manures and far in excess of the yields from plants grown *in the shade*.—F. Ransom and H. J. Henderson, Int. Cong. Applied Chemistry, 1912. This is of especial interest more particularly as *Belladonna* and *Digitalis* are frequently found in nature in partially shaded situations. Indeed, it has been advised to grow *Belladonna* in the shade. The results also are exactly analogous with the author's cultivation of *Digitalis*. He has found (*cf.*, "*Digitalis* Assay") that plants grown in the sun were the most active both by chemical and physiological assay.

Belladonna leaves grown in the shade contained 0.35% total alkaloids,—those grown in the sun 0.4%.—W. Unger, Y.B.P., 1913,261.

Direct sunlight favours leaf development and alkaloidal content.—Comptes Rend., 1922,174,183; Y.B.P., 1922,3.

Plants grown in obscurity show *increased* alkaloid content in leaves and stems with slight diminution in roots. Protein content of leaves increased by keeping in the dark.—J.C.S.A. i./22,96.

Plants grown in the hard climate of Scotland gave a good alkaloid figure—up to 0.58 per cent. Roots 0.72 to 0.78% (U.S. 0.45%), Stalks 0.08%.—R. Glode Guyer, P.J. i./21,169.

Artificial Manures, *e.g.*, Sodium Nitrate 1 cwt., with Kainit 3 cwt. per acre, increase the yield of *green plant*. This yielded $13\frac{1}{2}$ tons per acre September, 1911, as against the plot with no manure, but sun, $8\frac{1}{2}$ tons per acre.—Ransom and Henderson, *ibid.*

Basic Slag 2 cwt. per acre and Superphosphate (5 cwt.) applied March to April had good effect on alkaloid yield,—better than farmyard manure. The highest percentage of alkaloids has been observed in sunny seasons. Cultivated plants yielded as much as 1.08% alkaloid.—F. H. Carr, Int. Congress App. Chem., C.D. 1912, p. 432; Y.B.P. 1913.

Indian Government Belladonna grown at a high elevation (6,500 ft.) in rich virgin soil contains high percentage of alkaloid.—E. M. Holmes, P.J. ii./18, 103; i./19, 2. Evans found in the leaf 0.41% alkaloid and in the root 0.4%.

Cultivation in Kumaun (North West Provinces). Ten tons of fresh leaves picked during the year ending March 21/20.—Norman Gill, C.D., 1920, p. 1400.

Eptirix Atropæ Foudras. A small beetle has made its appearance in Belladonna plants at Hitchin, especially prevalent in dry seasons. Recommendations are given for cultivation which would tend to eradicate the insect.—Perrédes, P.J. ii./10, 135.

Phytophthora Erythrosepica. var. Atropæ on Belladonna Root.—N. L. Alcock, P.J. i./26, 232.

Belladonna fruit, either ripe or unripe, contains 0.1 to 0.13% Alkaloids.—P.J. ii./09, 473.

Frogs' and rabbits' livers have the power of destroying Atropine. This is due to a soluble body resembling a ferment. None of the tissues investigated in the cat, rat and dog have any like power.—B.M.J. ii./12, 1099.

Elimination of a Belladonna preparation taken internally is rapid. It rarely produces poisonous effects in medicinal doses.—L. ii./10, 575.

Extractum Belladonnæ Viride (B.P. 1898).

This is now little used, being replaced by the *B.P.* '14 Dry (Alcoholic) Extract of the leaf. It is, however, still employed in Glycerinum Belladonnæ.

'Indian' Belladonna possibly a *Scopola* species, e.g. *S. lurida*. According to E. J. Waring a tincture made with the leaves of this plant 1 in 8 of alcohol administered to patients produced extreme dilatation of the pupils. The largest dose was 20 drops during 24 hours—in two cases causing blindness. Great caution necessary.—E. M. Holmes, P.J. i./17, 351.

BISMUTHUM.

Bismuth in Pharmacy—the metal and its inorganic derivatives. Bismuth alloys, some melting as low as 60° C., are used for fire alarm sprinkler devices.

Aluminium Bronze, made of Aluminium 92, Copper 5, Bismuth 2, and Silicon 1, is resistant of Cyanide. **Bismuth Bronze**, containing Bismuth, Nickel, Copper and Zinc, or Bismuth, Nickel, Copper and Antimony, or Bismuth, Nickel, Copper, Lead and Tin, is resistant of seawater.—G. Malcolm Dyson, P.J. i./28, 242, 348, 582.

Colorimetric estimation of Bismuth in urine by means of Phenazone and Potassium Iodide, after destroying organic matter.—C. A. Hill, L. ii./25, 1281.

A method of determination of Bismuth in body fluids and tissues.—C. S. Leonard, Jl. Ph. & Exp. Ther., July '26, 81.

Distribution of Bismuth in the blood.—B.C.A., '28, 1151.

Bismuth intramuscularly, as the metal in Dextrose solution, or Potassium Tartrate or Salicylate in oil, Bismuth causes definite and prompt diuresis in human subjects.—Jl. A.M.A. ii./28, 225.

Studies in the pharmacology of Bismuth salts.—C. S. Leonard, Jl. Pharm. and Exp. Therap., Dec. '28, 333-364.

Liquor Bismuthi et Ammonii Citratis. (B.P. '14)

We find it best to store in full moderate sized (stoppered) bottles, which contain sufficient for immediate use. Sterile materials and utensils should be used. The Liquor made and stored in this manner will keep good for years. The addition of 1 of chloroform in 400 parts is also useful. The solution of ammonia used must be quite free from tarry matter. Test for the latter by adding 2 to 3 Gm. of copper sulphate to the ammonia solution until it smells very slightly of ammonia; tar constituents will colour it.

Our experiments show that the *B.P.* 1885 method is best—is both economical and expeditious. It is important that the Bismuth Citrate should be pure.

In the *B.P.* '14 method more washing than that specified may be required. And if a large amount be used there appears liability to reform some subnitrate which will not dissolve in the Ammonia.

One mol. weight of commercial Bismuth Citrate requires approximately 2 mol. weights of Ammonia to dissolve to an alkaline solution. This Solution, on adding Citric Acid to neutralise $\frac{1}{2}$ a molecular weight of the Ammonia, becomes amphoteric to litmus. Therefore, 1 molecule weight of Citrate to make a Neutral (amphoteric) Solution requires $1\frac{1}{2}$ molecular weights of Ammonia.—*Cf.* note on preparation, Vol. I., p. 229.

In estimating Bismuth in Liquor Bismuthi it is a good plan to reduce with alkaline Formaldehyde solution, wash, dry and weigh precipitate finally as Bismuth Oxide.—P.J. i./28,270.

Bismuthi Carbonas.—Calcium is frequently present as impurity.—H. Stout, P.J. i./21,73.

Manufacture of 'Light' Bismuth Carbonate a trade secret. During conversion of Bismuth Subnitrate to Oxy carbonate adsorption of traces of alkali results and no amount of washing will remove it. With tap-water double decomposition between this alkali and Calcium salts occurs, with consequent deposition of Calcium Carbonate. Method must be used to destroy the alkali: it is not stated what method.—R. W. E. Stickings and H. C. Coupland, C.D. i./28,605.

Bismuthi Hydroxidum.—C. E. Corfield and Miss E. Woodward were unable to substantiate the formula BiO.OH for a body made by the FR. CX. or other method. The only pure compound they could obtain was one of the formula Bi(OH)_3 .—P.J. i./24,83.

Bismuthi Salicylas.

Bismuth in organic compounds, Salicylate, Liquor, Xeroform, etc., is easily estimated by reducing to metallic Bismuth with Formaldehyde.—S. B. Tallantyre, B.P. Conf., 1919.

5 Gm. treated with 50 Cc. of dry ether should yield not more than 0.005 Gm. Salicylic Acid.—B.P. '14.

Rectified Benzol as extractive. If allowed to percolate through the sample and the liquid be dropped into dilute Ferric Chloride Solution, this will detect the smallest quantity of free Acid by violet colouration at junction of the two liquids. Alcohol decomposes it. Chloroform is unsuitable.

Bismuthi Subnitrates.

Dragendorff's Test for Alkaloids.—Bismuth Subnitrate 8, Nitric Acid, Sp. Gr. 1.18, 20; add this solution gradually to a concentrated solution of Potassium Iodide 22.7. Cool, decant from Potassium Nitrate formed and dilute to 100 with water. The solution precipitates most alkaloids.

A suggested modification.—Dissolve Bismuth Carbonate 64 in Hydrochloric Acid 85 and add Water 500 containing Potassium Iodide 166. Finally make up with Water to 800. This eliminates Nitric Acid which causes decomposition, and the proportion of Potassium Iodide is less. With this formula there is not the trouble with the crystals of Potassium Nitrate.

HYPERTENSION—Administration of Bismuth Subnitrate assists materially in obtaining a reduction in arterial tension, owing to its property of breaking the vicious circle of vascular fatigue, hyperirritability, with more spasticity and fatigue, and thereby permitting of physiologic rest.—E. J. Stieglitz, JI. Pharm. & Exp. Therap., Dec. '28,422.

Thresn's Reagent.—Bismuth Citrate 2.4 Gm., Water 20 Cc., Ammonia *q.s.*, made up to 30 Cc. with Water and add to a solution of Potassium Iodide 2 Gm. in Nitric Acid 45 Cc. Is similar in use to above.

Metallic Bismuth is diamagnetic. It is a bad conductor of heat. It is used in making sterco-metal on account of its low fusion point—about 300° C.

Nitrate is estimated in Bismuth Salts by mixing 5 Gm. of the salt with 5 Cc. Alcohol, 150 Cc. water, 50 Cc. 33% Caustic Potash and 8 Gm. Devarda's Alloy, and, after standing 10 minutes, the Ammonia formed is steam-distilled and titrated—using Methyl Red.—T. McLachlan, P.J. i./21,477.

Sodium Potassium Tartro-Bismuthate.

Maximum tolerated dose intramuscularly in rabbits is 100 mgr. per kilo. It and others tested produce necrosis of kidney tubules, with attendant nephritic and uræmic symptoms.—Leonard and O'Brien, JI. Pharm. & Exp. Therap., July, '26, per C.D. ii./26,943.

Bismuth Anhydro - methylene Citrate, Diethylmalonate, Mandelate, Vanillate and Cinnamate made with help of Bismuth-Mannitol solution

obtained by grinding together Bismuth Nitrate Cryst. (1 mol.) and Mannitol (1 mol.) and treating the mass with water.—J.C.S.A. i./20,9.

Organic derivatives of Bismuth. Preparation of derivatives of Quinquavalent Bismuth.—J.C.S., June, 20,762.

True organic Bismuth compounds with the direct Carbon-Bismuth linkage are too toxic for use.—G. M. Dyson, P.J. i./28,583.

BROMUM.

Br = 79.916.

The following medicinal inorganic **Bromides** contain the halogen in these proportions :—Ammonium Bromide (NH_4Br = 97.956) 81.58%, Calcium Bromide U.S. (contains 84% CaBr_2 = 200.902) 66.83%, Lithium Bromide (LiBr = 86.756) 92.10%, Potassium Bromide (KBr = 119.012) 67.17%, Rubidium Bromide (RbBr = 165.56) 48.3%, Sodium Bromide (anhydrous) (NaBr = 102.913) 77.67%, Strontium Bromide *Off.* ($\text{SrBr}_2 + 6\text{H}_2\text{O}$ = 355.558) 44.96% (if exsiccated about 64.60%), Zinc Bromide (ZnBr_2 = 225.21) 70.98%.

Of the **Organic Bromine Compounds** Brominol contains 10 and 33 1/3%, Bromural 36%, Bromalin 32%, Bromalbumin 7%, Brometone 77%.

In daily max. doses :

Brominol 33% (60 grains)	= 20 grains Br.
Bromural (10 grains)	= 3.6 " "
Bromalin (30 grains)	= 10.6 " "
Bromalbumin (10 grains)	= 0.7 " " (or more)
Brometone (15 grains)	= 11.6 " "

DETECTION OF BROMINE EXCRETED IN THE URINE AFTER TAKING VARIOUS BROMINE COMPOUNDS—SEDASPRIN, ADALIN, AND POTASSIUM BROMIDE.

Test for Bromine in Urine. The urine is made alkaline with Caustic Soda, evaporated to dryness and incinerated at a low temperature. The mass is extracted with about 10 Cc. and 4 Cc. of water filtered, acidified and a few drops of Chlorine Water added, and the mixture shaken out with 5 Cc. of colourless Carbon Bisulphide.

In an investigation we found :

A patient under Potassium Bromide.

Case I. [5 grains (0.3 Gm.) = 218 mgr. of Bromine].

5 grains were taken at night. The urine passed in the morning contained about 2 mgr. of Bromine, while the third quantity—16 hours after taking Potassium Bromide—was free from Bromine.

Case II. [10 grains (0.6 Gm.) = 435 mgr. of Bromine].

10 grains were taken at night, by a different person, the following results being obtained :—

In the evening no trace of Bromine was found in the urine. During first day : About 3-4 mgr. found in all the urine ; After 36 hours : About 2 mgr. found in urine ; 40 hours after taking : About 1 mgr. found ; 60 hours after taking : Only a very slight reaction.

In each separate quantity (varying from 250 to 500 Cc.) of urine examined only 2 to 3 mgr. or less of Bromine was found. This means that during the 2½ days probably **only about 20 mgr. of Bromine (5% of the amount taken was excreted** in the urine.

Cushny found that after a single dose of 30 grains of bromide the urine may contain traces of the drug for 2 months, only about 10% being eliminated in the first 24 hours.—J. H. Hannan, Pr., Oct., '27,262.

A patient under Adalin—[15 grains (1 Gm.) = 0.328 Gm. of Bromine].

The urine was shaken several times with Chloroform to remove any unchanged Adalin, but this would possibly not eliminate Diethyl-bromo-acetic Acid—a likely product of hydrolysis.

15 grains (1 Gm.) were taken at night. The urine passed in the morning was free from Bromine, but the third quantity examined (20 hours after taking) contained about 3 mgr. of Bromine. This may, however, have been present as $(\text{C}_2\text{H}_5)_2\text{C.Br.COOH}$.

Adalin is evidently not expected to split up since—"though containing Bromine, its action is attributed to the molecule as a whole."

A patient under Sedaspirin—[10 grains (0.6 Gm.) = 200 mgr. of Bromine].

After evaporation the urine was acidified and extracted with Ether several times to remove any Bromo-salicylic Acid and the test applied for inorganic bromide, but the results were negative.

In view of the fact that so little is found after 5 grains of Potassium Bromide—an almost equivalent dose in Bromine content—this was not surprising. The Bromine had been absorbed.

Fluorescein Test for Bromine in Body Fluids.

Soak strips of filter paper in a saturated solution of Fluorescein in 60% Acetic Acid, and allow to dry. Add to body fluid in a test tube a few crystals Potassium Permanganate. Agitate and add a few drops Concentrated Sulphuric Acid. Moisten Fluorescein paper with 2% Acetic Acid and hold at mouth of test-tube. Presence of Bromine indicated by rapid change of paper from yellow to bright pink. Presence of Chlorine and Iodine does not interfere with test. Found positive in urine voided 15 minutes after oral administration of 10 grains of Sodium Bromide. The Fluorescein papers will keep.—G. H. Belote, *Jl.A.M.A.* i./27,1697.

A method for the estimation of bromides in urine in the presence of large amounts of chlorides.—G. H. W. Lucas, *Jl. Ph. & Exp. Ther.*, Oct. '28,223.

Calcium Bromide.

In preference should be of the U.S. standard (containing not less than 84% Calcium Bromide and not more than 85%).—R. R. Bennett, *P.J.* i./28,563.

Method of Bromination with Aqueous Hypobromous Acid.

The use of hypobromous acid, prepared by digesting bromine and H_2O with excess of HgO , in the form of a straw-yellow solution containing about 6.2% of Br, is suggested as a brominating agent. It suffices to shake this in the cold with C_6H_6 ; $C_6H_5CH_3$, or C_6H_5COOH to obtain satisfactory yields of monobromobenzene, *o*-and-*p*-bromotoluene, *m*-bromobenzoic acid. Aniline yields tribromaniline; phenol gives tribromophenol under similar conditions; nitrobenzene resists bromination, as also does phthalic acid.—*J.C.S.A.* i./10,234.

CAFFEINA.

See also Vol. I., p. 248.

Caffeine and Theobromine fail to precipitate with Mayer's Reagent, distinguishing them from the majority of alkaloids. Caffeine has a bitter, not agreeable taste. Tea contains a minimum of 3.5% of Caffeine and a maximum of 4.0%. Raw coffee about 1.2% and when roasted about 1.3%. For manufacture, tea dust with the strongest yield of alkaloid is extracted.

TEA.—When there is neither caffeine nor tannin present in quantity exceeding that which the compound of them (caffeine tannate) contains, the tea is pronounced by the taster as of good quality. Caffeine and tannin occur mostly (in good teas) in the ratio of 1:3—which is virtually the ratio in Caffeine tannate.

TEA INFUSIONS.—Cold water extracts only a very small proportion of the total Caffeine in Tea, though solubility is 1.35 per cent. at 16° C. Caffeine is taken up always as Tannate.

Cup of Coffee.—The Caffeine in tea being in the form of Caffeine Tannate, is precipitated by the gastric juice and, therefore, the Caffeine is probably not absorbed until it reaches the alkaline alimentary tract. In the case of coffee, however, in whatever form the Caffeine may be present it is soluble in both alkaline and acid fluids and, therefore, the absorption in this case is probably in the stomach, hence the more prompt action as restorative.

Roasting Coffee diminishes the amount of Caffeic Acid. Infusion of raw coffee contains 9.6%, pale roasted 6.6%, and high roasted 3.7% approx. *Pyridine* is present in Coffee in small quantity. Coffee often relieves asthma—while *Pyridine* is advised as useful in asthma.

Caffeine, in its effects and constitution, is very like beef tea—though violently attacked in the past on the ground that through it men were losing their stature and women their beauty.—Prof. Dixon, *P.J.* i./24,66.

Benzol and Toluol are good solvents for extraction of Caffeine commercially from Tea Dust. Best to add Sodium Carbonate in the process.—*Y.B.P.* '23,6.

Decaffeinated Coffee.

The amount of Caffeine removal in current specimens approximates well over 90%, assuming that 1.2% of Caffeine by weight was originally present.—*A.M.A.* ii./28,883.

Caffeine injected subcutaneously or intravenously in 1 to 2 Gm. doses in dogs invariably caused rise in blood sugar, 7 out of 10 animals dying within 30 minutes to 13 hours. Simultaneous injection of **Caffeine and Insulin** invariably caused hypoglycæmia. The hyperglycæmic action of Caffeine may be due to its stimulation of the suprarenals and excessive production

of Adrenalin, thus proving the antagonism between the suprarenals and the pancreas in regulation of amount of blood sugar.—B.M.J.E. ii./24,84.

On the coronary vessels Caffeine, Theobromine and Theophylline claimed to have active vasodilator action, Caffeine being the weakest and Theobromine the strongest. In angina pectoris coronary vasodilation by the latter may be of service.—R. St. A. Heathcote, Jl. Pharm. & Exp. Therap., Dec. 1920.

Estimation of Caffeine in presence of Acetanilide, e.g., in headache powders; extract from a sulphuric acid solution with chloroform. Precipitate with iodine and decompose the periodide with sodium sulphite, and extract the base again with chloroform.

Determination of Caffeine in Caffeine-Sodium-Salicylate.

P.G. VI. directs to dissolve 0.5 Gm. of Caffeine Sodium Salicylate in 1 Cc. water in a 50 Cc. measure. Add to the solution 25 Gm. of Chloroform and 2.5 Gm. of Sodium Hydroxide solution. Shake thoroughly for 5 minutes. After adding 0.3 Gm. of Tragacanth, shake again for several minutes, and after a further 5 minutes pour 20 Gm. of the Chloroform solution (equivalent to 0.4 Gm. of the sample) through a little wool into a weighed flask. On evaporating the Chloroform and drying the residue at 100° C., the residue must be at least 0.16 Gm., representing 40% of Caffeine.

Caffeine hinders germination of seeds.—L. i./12,666.

Maté. (See also Vol. I, p. 253).

Analysis showed Caffeine 2.02%, Sugar as Glucose 6.08%, Tannin 11.22%—3 and 10 minutes infusion (the 10 minutes being on the old marc) at about 90° gave total dissolved substances respectively 21.8%, 31.8%, organic matter 19.4%, 28.4%. Mineral Matter (Ash) 2.4%, 3%, Tannin 7.68%, 11.08% and Caffeine 1.39% and 1.70%. The second figures in each case indicating totals.

The best method of preparing the 'Tea' is by first moistening the leaf thoroughly with boiling water, and then after a few minutes, adding the remainder of the boiling water and allowing to infuse for 15 minutes.

A mild heart stimulant if taken periodically. Leaving it off after having taken it for some time may, it is said, cause prostration. Mortality from heart disease in Argentine is greater than elsewhere—asccribed to Maté.

More than 18,000,000 people in S. America drink Maté. Thought to ward off rheumatism and produces exhilarating yet soothing effect on nerves and has very sustaining properties. Principal beverage of rural working-classes in the Argentine, Paraguay and Brazil.—Jl. Trop. Med., Sept. 1, '25, 320.

CALCIUM.

Calcium Metal.

The method of manufacture consists in electrolysing fused calcium chloride with an iron cathode which only just touches the surface of the salt and can be moved outwards so as to produce ingots of the metal. Its density is 1.548, M.Pt. 810° C. Can be drawn out into a very fine wire, being tenacious. Is only slightly acted upon by water, but combines with hydrogen and with nitrogen.

Calcium may be estimated *volumetrically* by precipitating it under specified conditions with excess of Ammonium Oxalate, the excess of which is subsequently titrated in the filtrate by means of Potassium Permanganate.—Abst. Ann. Rep. Chem. Soc. 1919 (Vol. XV.), p. 136.

Calcium Carbide. $\text{CaC}_2 = 64.07$.

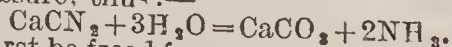
(Requires special storing.)

Grey masses, becoming white when moist. Evolves acetylene when brought into contact with water. May be used as a test for, and in the preparation of absolute alcohol.

Nitrogen Fixation.

When nitrogen is passed over calcium carbide heated to 1000° C.

Calcium Cyanamide, Syn. "***Nitrolim**" (T.M. 437595) $\text{CaCN}_2 = 80.086$, is formed. $\text{CaC}_2 + \text{N}_2 = \text{CaCN}_2 + \text{C}$. The nitrogen of same interacts with water under pressure, thus:—



The nitrogen must first be freed from oxygen. This is effected by fractional distillation of liquid air.

The above method of fixing atmospheric nitrogen is the **Frank-Caro** process. For details of manufacture see P.J. i./16,45.

Calcium Cyanamide, is a black powder, containing 15-20% Nitrogen and about 20% free Lime. As a fertiliser it is valuable on acid or 'sour' soils and is usually treated with oil to render it granular and to reduce its dusty and corrosive nature.

Another method—the production of Calcium Nitrate is that of **Birkeland-Eyde**.

A third is the production of nitrous fumes by passing air through an iron tube in which an alternating current arc of 5 metre length is maintained under a pressure of 4,200 volts.—**SCHOENHERR** and **HESZBERGER**. The gas obtained is mixed with limestone, forming Calcium Nitrate, the 'Air Saltpetre.'

For some years prior to 1914 Germany had been making *Cyanamide* on a limited scale and not long before the outbreak of war the Haber process for producing Ammonia by direct union of Hydrogen and Nitrogen had reached the stage at which its success as an industrial process was assured. In addition Germany possessed Ostwald's Process for converting Ammonia by oxidation into Nitric Acid. Our supplies of Ammonia on the other hand were restricted by the output of our gas works and coke ovens and we were entirely dependent for Nitric Acid on the import of Sodium Nitrate. The synthetic production by Germany of Nitric Acid during the war was a remarkable achievement.—**Sir J. Dobbie**, Pres. Add. J.C.S., Apl., '20, 430.

The first person in this country to direct attention prominently to the development of the Fixed Nitrogen industries abroad was **Prof. A. W. Crossley**.—**P.J. i./10, 329**.

Hydrogen from Coal and Nitrogen from the Air to produce **Ammonium Sulphate**.—Works in Cumberland.—**L.i./20, 210**.

In 1913, the **Badische Anilin- und Soda-Fabrik** produced some 20,000 tons of synthetic Ammonium sulphate, and by 1918 single units were making 20 tons per day of anhydrous Ammonia. The total German production of anhydrous Ammonia for 1918 must have exceeded 250,000 tons.—**Industrial Catalysis**.—**Stanley J. Green** (**E. Benn, Ltd.**).

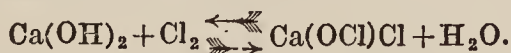
Calcii Chloridum.

Calcium Chloride is a by-product in the alkali industry and thus makes a cheap brine for refrigerating purposes. Super-saturated solutions are used in foot-warmers, the liquid on solidifying giving out a continual supply of heat.—**C. & D. i./25, 331**.

"**A. R.**"—Should be clearly soluble in water and neutral. For Barium and Strontium 1 Gm. in 10 Cc. of water should not show any turbidity after adding 20 Cc. of Calcium Sulphate solution and standing several hours. For Iron and heavy metals 1 Gm. in 20 Cc. of water and 5 drops of Ammonia solution should not show darkening or discoloration on adding 5 drops of Ammonium Sulphide solution. For Nitrate 0.1 Gm. dissolved in strong Sulphuric Acid should not give a blue colour on adding Diphenylamine Reagent—*q.v.*

Calcium Chloride given in excess may cause clotting of the blood.

Calx Chlorinata.—According to modern views, when moist CO_2 acts on bleaching powder Chlorine only is given off (no Hypochlorous Acid as originally taught). Air free from CO_2 very slowly liberates Hypochlorous Acid, but no Chlorine. With air containing CO_2 a mixture of Hypochlorous Acid and Chlorine is obtained, the proportion of the former decreasing with time. These points are explained on assumption that the action of Chlorine on alkalis is reversible



The action of air in promoting bleaching is therefore due to removal of Lime from the powder by CO_2 . The bleaching action is further accelerated by the addition of Common Salt or Calcium Chloride.

Stabilized Bleach, *i.e.* Bleach mixed with 20% powdered quicklime, retains its available Chlorine in hot climates, *e.g.* a sample leaving England at 25% and arriving in Madras showing 18.4%, fell to 10% in 42 weeks, while ordinary Bleaching (leaving England 35%) fell to 0.42% in 14 weeks. After 2 years, however, it was found to contain 5.9% Calcium Chlorate—this would not do for sterilising water, owing to its taste.—**A. F. Macculloch**, **J.S.C.I.** '21, 40, 240T; **Y.B.P.** '22, 119. 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

Water Sterilization with Chlorine and Chlorinated Lime. See Vol. I., p. 45, and the Water Analysis Chapter this Volume.

CAMPHOR.

Camphor Production.—The leaves are the best parts of the tree to use. The yield is 1% or more of crude Camphor.

Camphor Estimation (in Spirit of Camphor). Place 10 Cc. in a conical flask (= 1 Gm. Camphor) and add 4 volumes of Lead Subacetate Solution (Sp. Gr. 1.320) and shake. The Camphor collects as a cake on the top. The liquid contains some more in suspension. Filter in a cool place (covered). Wash flask with Ether and pour this on the filter, then wash with more Ether until all Camphor is extracted, collect Solution in a tared dish. Evaporate spontaneously, place in desiccator and weigh.

Synthetic (Artificial) Camphor is manufactured by acting on turpentine with various acids.

Natural and synthetic Camphor. The manufacture of Celluloid takes 80% of the world's production. The film industry takes a lot. The manufacture of synthetic Camphor is difficult economically—dependent on a plentiful supply of Turpentine rich in Pinene and its market value. One type competes against the other. Darbois has produced the synthetic of optical activity equivalent to the natural.—C.D. ii./26,405. See also P.J. i./24,234.

Pinene ($C_{10}H_{16}$) is obtained by fractional distillation of oil of turpentine previously freed from resin. The pinene saturated with dry hydrochloric acid is the old-fashioned artificial camphor. The subsequent processes consist of splitting off the hydrochloric acid to obtain camphene, which is isomorphous with pinene. This substance, dissolved in glacial acetic acid, with a little sulphuric acid, yields bornyl acetate, and this saponified becomes borneol, which is identical with Borneo camphor. After oxidation synthetic camphor results, and this corresponds exactly with the Japanese and Chinese camphor, except in optical properties.

The synthetic is optically inactive, therefore is not official. The B.P.'14 body is dextrorotatory, and a test for Artificial Camphor is also given in Spiritus Camphoræ. Synthetic Camphor has M.Pt. $165^{\circ}C$., whilst natural has M.Pt. $175^{\circ}C$.—*cf.*, also Ph. Ital.

Synthetic Camphor should be examined for halogens, usually due to Pinene Hydrochloride, Fir Camphene and other allied impurities.—P.J. ii./24,608.

Camphor Compounds: Homocamphor, a substance differing from Camphor in the inclusion of an additional CH_2 group in the ketone ring.—A. Lapworth & F. A. Royle.—J.C.S., June, 20, 743.

An isomeride of Camphor, 3-methyl-5-isopropyl- Δ^2 -cyclohexenone, possesses the physiological properties of Camphor to a high degree, and is also easily soluble in Sodium Salicylate solution. It has been introduced into therapeutics under the name of "Hexeton."—J.C.S., A.i./25,685.

☞☞☞ CANNABIS INDICA. (B.P.'14).

See also Vol. I., p. 266.

☞☞ Since February 26, 1925.

In Northern India the resin exuded is mixed with tobacco and smoked, or taken in the form of bhang as a drink. The native then passes into a state of languid ease, accompanied by an elated sense of superiority. There is also induced an altered relationship to time and space, so that minutes become hours and feet furlongs.—W. E. Dixon, C.D. i./28,747.

B.P.'14 requires that the drug should yield not less than $12\frac{1}{2}\%$ extract to 90% alcohol and Ash not more than 15%.

A pharmacological study of *C. Americana*, i.e., *C. Sativa* grown in America, showed that the former is quite as active as that imported. Determination of physiological activity by internal administration to selected dogs is reliable when the standard dose 0.010 per kilo body weight, is tested in comparison with the same quantity of a preparation of known strength.

☞☞☞ Extractum Cannabis Indicæ (B.P.'14.)

When this extract is dissolved with alcoholic solution of potassium hydroxide, and the solution evaporated to dryness, dissolved with water, and shaken with ether, the uncombined and unsaponified portion is in solution. On evaporating the ether and warming the residue with five parts of concentrated nitric acid the residue is almost entirely converted into a crystalline substance. If the alkaline liquor is now rendered acid with hydrochloric acid and shaken with ether the resin acids and chlorophyll are dissolved. The ether may be

completely evaporated and the residue dried and weighed. If we call the first active extract "A" and the second "B," in a genuine preparation A=44 per cent. and B=30 per cent., but at present what the minimum percentage of A is, which a genuine extract ought to yield, is undetermined.—D. B. Dott, C.D. i./22,117.

Pharmacological Examination.

U.S.P.X. tests by comparison of degree of incoordination produced in dogs by 0.1 Cc. per kilo by the mouth, with that caused by the same dose of a standard preparation.

The effect produced in dogs is like alcoholism in man. There is at first slight loss of control in the hind legs so that the dog staggers, later the ataxia is more marked—the dog is unable to stand up and begins to show drowsiness and may finally pass into heavy sleep.

Test for recognition of Hashish.

The suspected material is extracted with petroleum ether of low boiling point. This extract, filtered, and evaporated to dryness. Both extraction and evaporation should be carried out in the cold. In presence of a considerable quantity of hashish a marked amount of tar-like residue is obtained, but it is sufficient for the reaction if only a faint yellow stain is left. To the residue a weak alcoholic solution of potash or soda (about N/10) is added and the liquid allowed to evaporate at room temperature. In presence of hashish a rich purple or reddish purple colour develops, which, on dilution with water, takes on a more bluish cast. Hashish is frequently sold dissolved in fat or oil, and for such alcohol is best. Extract of Indian hemp (*B.P.*) and Ceylon samples did not respond. Samples of ganja, charas and majun from India and a plant grown in Egypt responded perfectly. The ordinary hashish sold in Egypt is largely of Greek origin, and of a large number of samples tested since 1909 not one has failed to respond. Soil, climate, cultivation, and curing influence the chemical composition. The following is suggested as a useful presumptive test to which hashish or other *Cannabis* preparations from India, Egypt, Greece, Sudan, and Uganda all respond. The petroleum-ether extract is made as usual, and the evaporation of the solvent is carried out in a short test-tube. To the residue is added a few cubic centimetres of a reagent prepared by saturating absolute alcohol with dry hydrogen chloride gas. In the presence of *Cannabis* extract the liquid strikes a bright cherry-red colour which disappears on dilution with alcohol or water. Trials were made with a number of plant extracts and over 200 alkaloids, glucosides, etc., but in no case was a similar reaction obtained. Certain volatile oils—*e.g.*, *origanum* and *santal*—give a similar reaction, but the colour is far less intense for similar amounts of material.—W. Beam, Wellcome Res. Lab., Khartoum, C.D. Jan. 1/16.

Criticism of the finding of *Cannabis* in tobacco (*cf.*, Vol. I., p. 874).—E. Griffiths Jones, B.M.J. ii./23,841.—The method of assay is provided in the P.J. ii./23,353, 383, 495, 523. The proportion of 1 drachm of the Official Tincture per ounce of Tobacco is correct.—R. L. E. Downer, B.M.J. ii./23,1006.

[P 1] CANTHARIS.

See also Vol. I., p. 267.

Cantharides should contain not less than 0.5% Cantharidin.—P.G. VI. has 0.7%. FR. CX. 0.4%. U.S.X. not less than 0.6%.

Assay process (Greenish); by extraction with benzene.—P.J. i./07,322 *et seq.*

Gaze's Assay process for galenical preparations of the drug: 50 Cc. of (for example) the tincture is evaporated to dryness with 25 Cc. of water and 1 Cc. of a 30% solution of Sodium Carbonate. The residue is taken up with 10 Cc. of water and 2 Cc. of 25% hydrochloric acid, the liquid transferred to a small separator and extracted with four separate portions of 10, 5, 5, and 5 Cc. of chloroform. The chloroform is evaporated at a low temperature, and the residue allowed to stand at ordinary temperature for twelve hours. It is then treated with two successive small portions of petroleum ether, each being poured on to a small filter, the residue and the filter washed first with water containing a trace of ammonium carbonate, then with pure water, and then dried at 50°. The portion remaining undissolved in the flask is treated with warm acetone, which is passed through the filter, which is further washed with acetone, and the brownish residue is dried on a water-bath to constant temperature and weighed.

CAOUTCHOUC.

See also Vol. I., p. 270.

Vulcanisation of Caoutchouc with Benzoyl Peroxide and Lead Oxide in presence of Di- or Trinitrobenzene.—J.C.S.A. i./20,244; see also *ibid* 245.

Synthetic Rubber.—Processes of manufacture depend on polymerising isoprene. According to Harries this is effected by heating with Glacial Acetic Acid in closed containers to above 100° C.

India Rubber is a condensation product of $C_{10}H_{16}$. This group is common to Turpentine and the terpenes, in many essential oils. Synthetic Camphor is made from Turpentine. Synthetic Rubber has been made from $C_{10}H_{16}$ in some form or other. Nature elaborates many useful things from this base.—L. ii/12,595.

For latest information on Rubber from cultural, etc., aspect, consult works advised by the "India Rubber Journal," London.

Plaster Mull Basis.—Melt White Wax 1 with Lard $3\frac{1}{2}$ with gentle heat and pour it slowly on to India Rubber Paste (1 in 10) 5 parts continually stirring until intimately mixed. The quantity of solids in this paste is 5 to 9½. To prepare a 50% Mullplast a quantity of medicament equal in weight in the solids in the paste must be added. Starch may be used in diluting, e.g. for the various strengths of Salicylic Acid.

The Salicylic Acid Mulls when originally introduced were found to be painful in use for the removal of cuticle and in treatment of skin affections. Creosote was therefore added.

India Rubber Paste is made by soaking India Rubber in Benzole. Rubber is better than Gutta Percha. Unvulcanised rubber is wanted.—A. W. Gerrard, B.P. Conf., 1920. In discussion it was said that the plasters would not keep. Nearly 30% of rubber is wanted.

CARBONIS TETRACHLORIDUM.

The following information is additional to that on *Ankylostomiasis*, Vol. I., p. 274.

Deaths after Carbon Tetrachloride have occurred in Jamaica, and **Thymol** is now the drug of choice against hookworms.—B. M. Wilson, B.M.A. Ann. Meeting, B.M.J. ii./28,207. Carbon Tetrachloride a proved potent liver poison and should not be given to a purged and fasting patient unless sufficient Glucose is given at the same time.—H. M. Hanschell, *ibid*. Of value by the mouth and intravenously in human schistosomiasis and in distoma infestation of cattle.—F. G. Cawston, *ibid*.

Not the ideal anthelmintic. In addition to the many deaths reported in the literature (some with doses as low as $1\frac{1}{2}$ Cc.) there are many unreported fatalities. No justification in morality, science, or expediency in the 'herd,' treatment of backward races.—Clayton Lane, B.M.J. ii./28,195.

CASCARA SAGRADA.

See also Vol. I., p. 276.

As to the extinction of *R. Purshiana* from its habitat in British Columbia, Washington, Oregon, and N. California, opinion seems divided. Some say the stumps of trees, which are sufficiently exposed to sunlight will send up shoots which in time develop into trees of commercial dimensions—if not in the sun, the stumps will die. A useful investigation in the Dept. of Chemistry, University of British Columbia, to find out whether the wood of the tree could be made to serve in place of bark, to determine also the presence of active Glucoside, and to see if ageing could be effected by Hydrogen Peroxide, was sent to us:—

Extracts of the wood were found to be 71% as effective as those from bark. Only some of the trees gave an extract with gripping properties. This was improved by oxidation with Hydrogen Peroxide. (The action of H_2O_2 said to be equivalent to the customary 3 years' storage.—P.J.i./24,41.)

The active principle does not appear to be a Glucoside. Mention is made of the **Manganese** No. of the ash in the case of Bark Extract. The average was 340, and in the Wood Extract 201. Total solids for Bark Extract 27.4%, and for Wood 4.69%. It is, in short, a commercial proposition, if the liquid extracts of the wood were made two or three times as concentrated as those from bark.—R. H. Clark and K. R. Gillie, Vancouver Med. Assn. Bulletin, Oct. '25.

Substitutes.

The bark from Texas, Arizona, Colorado, and New Mexico is sometimes substituted by or mixed with the bark of *Rhamnus Californica*, which is of a greyer tint externally, and the transverse section is less dark and more yellow than *R. Purshiana*. An inferior variety, known as Winter Bark, is cut from the steamed branches and is therefore in the form of chips.—C. & D. i./25,560.

Cultivation in British Isles. Trials have been made at various stations. About 35% of the seeds planted in 1908, amongst the most successful trials, were fertile. The seeds should be removed from the stiff pulp (dried fruit). Seems to prefer light to heavy soil. Can be raised by cuttings 3 to 4 inches long. Bark should be removed between end of May and end of August. Scottish soil and climate quite suitable for growing the trees.—A. McCutcheon, P.J. i./21,72; C.D. Jan. 29, '21, p. 151.

The names BARBERRY and BEARBERRY, misapplied to Cascara, have caused confusion in the States of Washington and Oregon and in British Columbia. Genuine Cascara grows usually with Red Alder (*Alnus rubra*), the Giant Cedar (*Thuja plicata*) and the Douglas Fir (*Pseudotsuga mucronata*). There have been ruthless methods of collection of the bark, especially during the war. The Dominion Department of Agriculture at Sidney, Vancouver Island, carefully watching the industry.—P.J. i./24,530.

The actual purgative body in Cascara is unknown. Tschirch isolated a principle anthra-gluco-sagradin, and similar principles from Rhubarb, Senna and Rhamnus.

Oxymethylanthraquinones are characteristic constituents of purgative drugs from widely separated natural orders, e.g., Rhamnus (*Rhamnaceæ*), Cassia (*Leguminosæ*), Quassia (*Simarubaceæ*), Aloe (*Liliaceæ*).

The characteristic aperient action is not due to Emodin. Emodin is, however a constituent, but chrysophanic acid or chrysarobin could not be found. Apparently there are no chemical differences between one and three year old ('matured') bark. This was said to exhaust a ferment and to moderate the griping action which the fresh bark possesses.

The larger proportion of Anthraquinone derivatives in Cascara are in the combined form. The U.S.P. fluid extract contained 0.4%. Fluid Extracts of commerce contained 0.17% and 0.24%. Debittered contained 0.07%.—Jl.Am.Ph.A., Oct., '26, per C.D. ii./26,931.

The refractive indices of commercial fluid extracts of Cascara Sagrada found to agree with the specific gravity and amount of extractive. The refractive index would be useful in indicating that the extractive of galenicals is free from extraneous matter.—C.D. ii./09,185.

CERIUM. Ce=140.25.

This element, in addition to lanthanum and didymium, occurs as silicate in Cerite and as phosphate in Monazite, also in Samarskite and Gadolinite. Monazite is a mineral of fairly wide distribution in Brazil (in the State of Rio de Janeiro). For details vide P.J. ii./09,492. Cerium has Sp. Gr. 6.7, Lanthanum 6.1, and Didymium 6.5. The last mentioned has been split up into Praseodymium = 140.92 and Neodymium = 144.27. Cerium possesses a variable valency. It is, like aluminium, either trivalent, or in some compounds apparently tetravalent, or even hexavalent as in the peroxide CeO_3 , in this respect differing from the majority of the rarer earth metals and resembling the elements which are known to possess physiological action, for example iron, arsenic, antimony and iodine. Cerium oxide is contained in incandescent gaslight mantles. The filament in Nernst lamps is said to contain zirconia and yttria.

Action on B. Tuberculosis.

Grenet and Drouin established that Cerium salts reduce fats of tubercle bacilli in cultures and produce a mononuclear leucocytosis. The salts are given intravenously, 2 to 5 Cc. of 2% solution for 20 days: rest for 15–20 days: followed by second and third series of injections. Patients improved and bacilli disappeared from sputum, but treatment of value only in afebrile cases. Evidence so far presented of little significance.—W. E. Dixon, B.M.J. i./25,814.

For details of Cerium Oxalate, Sulphocarbolate, etc, vide Vol. I., p. 849.

Titanium Compounds.

Titanium Metal. The best result in manufacture was obtained by reducing Titanium Chloride (TiCl_4) with Sodium by heat in a steel bomb. Titanium, practically 100% pure, was obtained. Sp. Gr. of the metal is 4.5 (Moissan found 4.87). It is brittle in large pieces when cold, but is remarkably malleable at a dull red heat.—Chem. News, May 20, 1910, 232.

Titanic Chloride, TiCl_4 , is kept in sealed tubes. It reacts violently with water and forms a white precipitate (an Oxychloride no doubt). On adding Ammonia complete precipitation of the Hydroxide occurs.

This body is not soluble in Citric or in Tartaric Acid or in Potassium Bisulphate.

Liquid Titanium Chloride hydrolyses quickly in moist air with a dense white smoke and is used for smoke-screens, sky-writing, etc.—F. P. Stroup, Am. Jl. Pharm., Aug., '28, 504.

Titanous Chloride, TiCl_3 , supplied in 15% solution (pale yellow in colour). Addition of Ammonia causes buff precipitate.

Titanic Oxide, TiO_2 . A white powder, extremely insoluble in ordinary solvents. It does not dissolve in boiling Nitric Acid or Aqua Regis. Used as a white pigment in place of 'White Lead.' RUTILE is the ore Titanium Dioxide used in leather dyeing.

Titanous Sulphate, $\text{Ti}_2(\text{SO}_4)_3$, (usually supplied in 15% solution with excess acid). A brown liquid employed as reducing agent.

Ferro-Titanium, an alloy with Iron, is largely used as a 'scavenger' for Oxygen and Nitrogen in steel manufacture. The only element that burns vigorously in Nitrogen.

Titanium-Ferrocyanide, in a fine powder, is a green pigment used as a substitute for Arsenical Greens in wall-paper manufacture.

In attempts to produce a **neutral organic Titanium salt** we found that Titanous Sulphate does not precipitate with Sodium Citrate, but the following is no doubt a definite Ammonio-Sodium-Citrate: Titanous Chloride solution (15%) 10 Cc., Sodium Citrate 1 Gm., add Ammonia *q.s.* to neutralise. The solution may contain Titanous Citrate, Sodium Chloride and Ammonium Citrate.

Hafnium (after *Hafniæ*, an ancient name for Copenhagen). A new element homologous to Zirconium and apparently present in specimens of Zirconium minerals to the extent of possibly one per cent. Discovered by means of its X-ray spectrum.—Na., Jan. 20/23.

(P) CHLOROFORM.

See also Vol. I., p. 284.

Historical.—

Discovered by Soubciran 1831, named by Liebig Trichloride of Formyle. 1832, re-named Chloroform by Dumas, 1834. Tried as an anæsthetic Nov. 4, 1847, by Simpson, upon himself, who communicated results to the Med. Chir. Soc. Edinburgh, Nov. 10, 1847. *Vide* C.D., Dec. 21, 1912; B.M.J. i./13, 41.

The credit is due to Simpson. The claims made on behalf of D. Waldie are not borne out by his own statement.—B.M.J. i./15, 1058, 1103.

Chloroform is now largely prepared by the action of chlorinated lime on acetone, as well as from both methylated and duty-paid alcohol.

A. D. Waller found by experiments on striated muscle that the physiological power of chloroform is 12 times that of ether and 100 times that of alcohol.

Future of anæsthesia. A good review of pioneers and sources of progress.—S. Johnston, B.M.J. ii./26, 775.

Chloroform Poisoning.

Glucose is useful in delayed poisoning following chloroform inhalation. In one case—a boy who had taken chloroform upon a previous occasion without detriment—recovered under a mixed treatment of alkalies and glucose.

Adrenalin in Chloroform Anæsthesia.—Death followed injection of 5 minims of Solution (1 in 1,000) with light Chloroform anæsthesia in an operation for deflected nasal septum. When Chloroform anæsthesia is deep the danger of injecting Adrenalin is less than when light.—B.M.J. i./13, 879. It should

not be given to a patient under Chloroform.—*Ibid*, p. 704. Death probably caused by Adrenalin getting into the blood stream.—B.M.J. i./13,1023.

General anæsthetic not necessary.—*Ibid*, p. 1350.

Chloroform is toxic for heart muscle. Adrenalin is contraindicated wherever Chloroform is employed and *vice versa*.—W. J. R. Heinekamp, *Jl. Pharm. and Exp. Therap.*, Nov. 1920.

Chloroform per os. Numerous cases are on record of swallowing Chloroform intentionally and through error—with recovery usually under Strychnine.

B.M.A. DISCUSSION ON DOSIMETRIC ADMINISTRATION OF CHLOROFORM.—2% of Chloroform under normal conditions has not led to dangerous consequences. Must be supplied continually in 1 or 2% strength.—B.M.J. ii./10,751, 754,784,797.

The effect of Chloroform anæsthesia on blood, kidneys and liver of young children is very slight—with proper supervision, a good anæsthetic for children.—B.M.J.E. i./24,43.

In determination of the **Boiling Point** of chloroform it is important to transfer about the last 15% in the flask into a smaller flask or tube, otherwise it will be found in practice that this portion may refuse to pass over below 65 to 70° C.

Test for Decomposition of Chloroform:—

Small pieces of Pith steeped in Congo Red Solution. Acidity would cause the Congo Red dye to change to blue.

“A. R.”—For *Chlorine* shake 5 Cc. with 10 Cc. of water. Add a few drops of solution of Cadmium Iodide to a portion of the aqueous layer removed and then starch paste. There should be no blue colour.

Chloroform is stated to be absorbed by the corpuscles rather than by the plasma of the blood. ‘Carius’ analyses are best for estimating.—In chloroform narcosis the transport of chloroform from and to the lungs is a function of the red corpuscles.

Colorimetric estimation of small quantities in solution (0.1 to 0.0001%) in animal tissues. A pink powder is obtained on heating a solution with Pyridine in presence of Sodium Hydroxide.—W. H. Cole, *Jl. Biol. Chem.* '26,173.

Tetrachlorethane is also known as Acetylene Tetrachloride and by the trade name of Celson. It is a good solvent of resins, Cellulose Acetate, etc. *cf.* Vol. I., pp. 293, 442.

CINCHONÆ CORTEX.

See also Vol. I., p. 295.

The cultivation of the Cinchonas is carried on in India, in the Nilgiri Hills in the south, and near Darjeeling in the north-east, also in Ceylon, Java, and Jamaica.

History and Development of the Cinchona Plant—see the Chapter on Quinidine, Quinine, etc., Alkaloids.

Introduction into Java (1852). An example of Dutch grit and perseverance. Java now provides about 90% of the world's supply of bark. Imperial importance of the situation.—E. M. Mellor, *P.J.* ii./22,327.

A very interesting account of the introduction of **Cinchona Cultivation** from Peru into India and the cultivation of *C. Callisaya* (from the seed of a native Indian tree) in Java in 1852 by the Dutch. They realised their mistake, however, in 1861 and started cultivation, but it was badly managed. In 1916 the great war showed the error of allowing a friendly Neutral to have monopoly in a *bark rich in Quinine*. Attention is again drawn to Maj. Acton's work showing that total alkaloids are as good as Quinine, and Indian bark supplies an equivalent amount of these. It was *bark* and not Quinine that started the fame of Cinchona from Peru.—M.D., L.P.S.I., C.D. 1920, 1447.

History of Cinchona. Varieties to grow for profit.—Sir David Prain, B.M.J. ii./25,963.

The optimum titration conditions for the Cinchona alkaloids, with advice on selection of Indicators.—C. Morton, B.P.C., 1926; *P.J.* ii./26,168; C.D. ii./26,235.

“Grey” *Cinchona* Bark from Huanuco found to contain Quinine 0.45%, Cinchonidine 0.22% Cinchonine 0.63% Amorphous Alkaloid 0.43%.

A further sample of S. American Bark contained 5.49% Cinchonine and only 0.027% Quinine. It consisted of *C. nitida* and other vars., and was also "Grey" Bark. The abnormal content of Cinchonine probably due to cultivation or growth at low altitudes and in hot moist atmosphere.—B. F. Howard and O. Chick, B.P. Conf., 1920.

Cinchona Bark Assay.

The B.P. process found to give erroneous results. The amount of water directed to be used is excessive, rendering the bark too wet, so that the alkaloids are not fully extracted by the Benzolated Amyl Alcohol.—P.J. i./25,265.

Alpha-Naphthol Test for Cinchona Alkaloids.—

Added to an Aqueous Solution of Quinine Sulphate, a few drops of fresh saturated alcoholic Alpha Naphthol Solution to which a few drops of Concentrated Sulphuric Acid (2 drops per Cc.) have been added, produces a yellow precipitate; when Reagent is in excess a yellow solution results. Quinidine, Cinchonidine and Cinchonine Sulphates act likewise. No other white alkaloids appear to give it. Cinchona alkaloids can thus be detected in presence of Atropine, Morphine, Cocaine, Strychnine, Caffeine, Brucine, Codeine and Antipyrine. A drop of the Reagent added to Chloroform or Ether residues of any of the Cinchona alkaloids gives yellow colour. We find this test to work satisfactorily.—Watson, Am. Jl. Ph. 1913,502; P.J. ii./13,881; C.D. i./14,84.

Extractum Cinchonæ Liquidum (B.P. '14).

The B.P. '14 method of making and of assay are unsatisfactory. The extraction is by no means complete—only 15 to 40% of the actual content in alkaloids are removed.—Oliver Chick, P.J. ii./16,144.

Nephelometric estimation of Quinine in blood and urine after administration in treatment, employing Tanret's Reagent. The ether used is purified so that it gives no reaction for aldehydes with Schiff's reagent or for Ketones with Scott Wilson's Reagent *q.v.* No turbidity must develop on shaking the ether with excess of the reagent.—I. J. Lipkin and W. Ramsden, B.M.J. i./18,560.

CINNAMOMI OLEUM (B.P. '14.).

A test to ensure absence of cinnamon-leaf and cassia oils is given—B.P. '14. Further, it should contain 55 to 65% of cinnamic aldehyde as determined by a sodium sulphite addition process. The Bisulphite is more commonly used, *cf.* other Pharmacopœias. It also contains from 4 to 8% eugenol and some terpenes.

Genuine oils frequently fail to dissolve in 1 in 3 of 70% Alcohol, but are usually soluble in 4 to 5 parts.—Finnemore (B.P. '14 says '3 to 4.').

Cinnamon Leaf Oil has Sp. Gr. 1.040 to 1.060, n_D^{20} 1.530 to 1.545, and contains Eugenol 70–90%, with only traces of Cinnamic Aldehyde and a little Benzoic Acid.

Neither Cinnamon nor Cassia Oil can be replaced as flavours by synthetic Cinnamic Aldehyde, although this constituent is contained to 70–90%.—Finnemore.

Details of *C. Zeylanicum*. Root, Bark Oil and Leaf Oil; *C. Cassia* and numerous others.—Bull. Imp. Inst., 1921, 19, 323; Y.B.P., 1922,63.

COAL TAR DERIVATIVES.

See also Vol. I., p.299 et seq.

Toluol.

Certain oil wells, notably in Borneo, yield a high content in this constituent. The fact was of vast importance in the war. It permitted the manufacture of T.N.T. on a relatively easy scale far in excess of the yield had the Coal Tar Distilleries been the only source of supply.

"T.N.T." Tri-nitro-Toluol. *Syn.* TROTYL, $C_6H_2CH_3(NO_2)_3 = 227.064$. Commercially it is seen as crumbs or granules or fine plate crystals. Melting point about 80° C. It is obtained by nitrating Toluol. Soluble in Acetone, Ether, Benzene, and Xylol.

As an explosive it has replaced Picric Acid. 'T.N.T.' is more stable and does not attack metals. When absorbed, mainly through the skin, it leads

no serious digestive trouble. It further induces hæmolysis and cyanosis. The brunt of the mischief falls on the liver.

Stomonal, consists approximately of Nitroglycerin 11, Ammonium Nitrate 57½, Sodium Nitrate 7, Sodium Chloride 20½, Wheat Flour 8½, Moisture 1. **AMATOL** is T.N.T. mixed with 40 to 60% of Ammonium Nitrate. Mixed with 20% it is **AMMONAL**.

T.N.T. and "Stomonal" dermatitis. A pigment of Camphor 2 drachms, Phenol 1½ drachms, Mercuric Chloride 15 grains, Picric Acid ½ drachm and Alcohol 6 ounces = 6 drachms, useful. Dabbed on by the medical man freely—not given to the patient—on inflamed and itching parts (not on irritable mucous surfaces). Especially valuable in the early pruriginous stages. For some use two ounces of the pigment mixed with a Calamine Lotion 4 ounces and ½ drachm of Acacia Gum added.—K. Prosser White, L. i./16,402; see also A. Livingstone-Learmonth and B. M. Cunningham, L. ii./16,261.

Ministry of Munitions on T.N.T. and poisoning. It produced 50 cases of fatal toxic jaundice out of many thousands of workers engaged. Account of dermatitis, digestive troubles, blood changes, and jaundice caused.—B.M.J. i./16,842; L. ii./16,1026.

Sodium Bicarbonate freely given; successful treatment.—B.M.J. i./18,450.

T.N.T. Effect on the blood. No adverse effect on the red cells and hæmoglobin. Appreciable increase in leucocytes. Cyanosis is common among workers—possibly production of NO-Hæmoglobin or methæmoglobin—P. N. Panton, L. ii./17,77.

Three grains in 1 grain doses taken experimentally. Urine becomes orange colour.—Walter Smith, B.M.J. i./17,618.

Tests for T.N.T.—In the free state a weak ethereal solution gives a deep red with caustic potash—preferably in alcoholic solution.

Webster's Test for detection in the urine. 12½ Cc. of the Urine mixed with an equal volume of Sulphuric Acid 20:100 and shaken with 10 Cc. of ether. The acid liquor is rejected and the ether washed once with 25 Cc. of water. Then treat this Ether solution with 5 Cc. of Alcoholic Potash Solution 4 or 5:100. When T.N.T. is present a purple colour is at once formed varying in intensity. Care must be taken to distinguish between absorbed T.N.T. and accidental contamination.—B. Moore, Medical Press, 1916, 153, 647. See also B.M.J. i./17,618 and especially L. ii./16,1029. Also modification to exclude possible errors through consumption of rhubarb, etc.—F. Tutin, L. ii./18,554.

T.N.T. poisoning—how it was tracked and prevented.—B. Moore, B.M.J. ii./21,721.

For further information on T.N.T. and other explosives see 'High Explosives'—E. de W. S. Colver, 1918; "T.N.T. and Mono- and Di-Nitrotoluene, their manufacture and properties"—G. Carlton Smith, 1918; and "Explosives," by E. de Barry Barnett, 1919.

Trinitro-Butyl-Toluene, $C_6HCH_3C_4H_9(NO_2)_3$ is synthetic Musk or Tonquinol, referred to, Vol. I., pp. 316, 871.

In artificial Musks, it is possible to replace the Nitro groups by CHO, OCH_3 , COCH₃, halogens and CN, without altering the odour, but the tertiary Butyl group, or the presence of tertiary Carbon is essential.—P.R. '24,360.

Methylene Blue (Medicinal).

See also Vol. I., p. 325.

N.B.—Distinguish carefully from the commercial article containing zinc chloride. Test for this by incinerating and dissolving the residue in dilute Hydrochloric Acid with the addition of Nitric Acid. On adding Ammonia in excess and passing H_2S through the solution there should be no precipitate.

Medicinal Methylene blue is preferable to the commercial for making alcoholic solutions for bacteriological staining, as being more soluble, cf. Löffler's Alkaline Methylene Blue.

Methylene Blue as Indicator in Iodometric Titrations.

When titrating with standard iodine, the usual starch indicator may be replaced by methylene blue. Use a solution of 0.05 Gm. in Water 1,000 Cc. 1 Cc. of this is added to 50 Cc. of the solution to be titrated. The end point is the change from blue to yellowish-green, but an indicator is hardly necessary in Iodometric titrations.—W.H.M.

Sahli's Pill.—To diagnose peptic activity of the gastric juice a pill of Methylene Blue is enclosed in catgut in the form of a so-called desmoid pocket

and swallowed by the patient after dinner. As soon as the catgut is dissolved Methylene Blue escapes and dyes the urine, the time required to effect this result furnishing a measure of the condition of the gastric secretion. The Methylene Blue may be enclosed in a small piece of rubber tubing tied with thin catgut—the knot being touched with shellac.

TESTS FOR PERMEABILITY OF THE KIDNEY.

For further consideration of Renal Function tests with significance of results see Urine Analysis chapter.

Methylene Blue Test.—1 Cc. of 1 in 20 solution is injected into the gluteus maximus and the urine is turned pale green in half an hour, the color increasing up to the fourth hour. Sterules of this strength are prepared.

The method is sufficient to compare the work of the two kidneys, but the Indigo Carmine method is better.

Indigo-Carmine Test.—Indigo-Carmine Sterules (*Intravenous*) contain 10 Cc. of a saturated solution (approx. 1%). Sterules are also made containing 10 Cc. 0.4%. For testing kidney permeability. Confusion has arisen as to the strengths of these solutions. They are given undiluted.

Cystoscopic examination of the ureteral openings and the urine gives, by depth of colour, indication of renal functional power.—L. i./o7,793.

The cystoscope should be introduced immediately after the injection and the ureteric orifices carefully watched, when the ejection should appear as a forcible dark blue jet. Parenchymatous or interstitial nephritis is suggested by delay in excretion from both ureters. Marked delay on one side indicates disease: thus, if 8 to 12 minutes after injection, suggests chronic pyelitis. If 12 to 18 minutes elapse before elimination partial ureteral obstruction or moderate impairment of renal function is indicated. 20 minutes' delay indicates almost complete obstruction, or serious disease of the kidney or ureter.—Urinary Analysis, L. Heitzmann. See also Choyce's Surgery.

Intramuscular injections (10 Cc. of 0.4%) have also been used. Here also confusion has existed concerning the strength employed. The colour should appear in the urine in 10 to 12 minutes if functional capacity is in order.

Best results obtained by giving a small quantity, 5 Cc. of 0.4% solution intravenously, the excretion of the dye beginning 4 to 5 minutes afterwards. If a larger quantity be injected the blue coloration is so intense that the cystoscopic medium becomes obscured and it may be impossible to discover any difference in the colour from the two ureters. A good elimination of the dye does not preclude a minute tuberculous lesion of the kidney.—J. Swift Joly, B.M.J. ii./27,847. See also H. Maclean, B.M.J. ii./21,426.

Collapse following intravenous injection of 2 Cc. 4% solution—actually a suspension. No concentration more than 0.4% should be used intravenously.—A. E. Roche, B.M.J. i./28,921; ii./28,778.

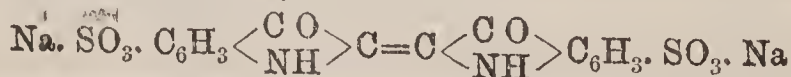
In normal kidneys the colour appears within 5 to 20 minutes, the maximum colour should appear in 45 minutes, and total excretion should be complete in 14 hours.—G. A. Harrison, L. ii./28,1144.

Tests of renal efficiency.—G. A. Harrison, L. ii./28,1092.

Indigo or Indigotin (natural) is obtained from the shoots of *Indigofera Tinctoria* (*Leguminosæ*) in India and Java, by maceration with lime and water. The pure substance has the composition $C_{16}H_{10}N_2O_2$. For chemical synthesis, *v. Indican*.

Indigo Carmine is the Sodium Salt of Indigotin—5.5%—Disulphonic Acid, which acid substance is Sulphate of Indigo, or Soluble Indigo prepared by adding gradually Powdered Indigo 1 to Nordhausen Sulphuric Acid 5 or Oil of Vitriol 8—the vessel being kept surrounded by cold water.

Indigo Soluble. FR. CX. has *Syn.* Sodium INDIGO-DI-SULPHONATE, INDIGO CARMIN, CERULEINUM.



Completely soluble in warm but only slightly in cold water. Soluble Indigo as mostly understood is the acid substance not the sodium salt.

The Sodium Salt is formed as a precipitate on neutralising Soluble Indigo with Sodium Hydrate. It has to be washed with a solution of the same salt—to remove excess of Sulphate of Indigo. The product is pressed and dried and is then soluble in water.

Isatin. $C_8H_5NO_2$. Yellowish red prismatic crystals obtainable by oxidising indigo with chromic or nitric acid, also by boiling o-nitro-phenyl propiolic acid with caustic soda.

Natural products versus synthetic methods.—The work in progress by Armstrong, Davis and others on natural Indigo may well re-establish the Indian Indigo plantations. It is by no means impossible that the day may soon come when vegetable oils produced in the tropics will be brought northwards for use as an economic form of fuel.—Sir William Pope, Society of Chemical Industry, C.D., 1921, p. 260.

Phloridzin Test.—This consists in injecting 5 to 10 mgr. of phloridzin (see also Vol. I., p. 877 and this Vol., *Urine Anal. Chptr.*) subcutaneously in 20 to 30 minims of water. Glucose should normally appear in the urine in half an hour.

For determining the diseased side of the kidney this test is also delicate.

The technique of Caspar's method consists in the subcutaneous injection into the buttock of 1 Cc. of 1% Phloridzin Solution and observation as to (a) excretion of sugar by a healthy kidney or (b) non-excretion at all or more slowly and to less extent (diseased).

Phenolsulphonephthalein $(C_6H_4.OH)_2.CO.C_6H_4.SO_2=354.176$.

A red crystalline substance slightly soluble in water, more soluble in Alcohol, insoluble in Ether. With alkalis it gives an intense purple red colour even in extreme dilutions.

Manufacture.—It may be prepared from Saccharin by hydrolysis and subsequent treatment of the anhydride of Sulphobenzoic Acid obtained therefrom with Phenol, *e.g.*, Saccharin 100 Gm. boiled with 1500 Cc. of water and 125 Cc. Concentrated Hydrochloric Acid until no longer sweet (4 to 6 hours), then evaporate to crystallise, collect crystals and evaporate the mother liquor to almost dryness and collect the crystals and dry them with the others. Distil the dried crystals thus obtained with an equal weight of P_2O_5 , this gives the anhydride of o-Sulphobenzoic Acid which is then fused with Phenol at $130^\circ C$. for several hours until combination is complete.—L. G. Rowntree and J. T. Geraghty, *Jl. Pharm. and Exptl. Therapeutics.*—Vol. i /1909-1910, p. 579.

May also be prepared by heating together Saccharin (1 mol.), Phenol (5 mols.) and Sulphuric Acid (4 mols.) at $120^\circ C$. for at least 48 hours. The dye is purified by repeated precipitation from Sodium Carbonate solution.—B.C.A., Sept., '28, 1003.

Phenolsulphonephthalein Test.—Technique.

An aid in proving whether the diminished excretion of Nitrogen is due to interference with function and also as a guide to the degree of interference with renal function in toxæmia of pregnancy and threatened eclampsia.

Give 300 to 400 Cc. of water half an hour prior to the test. Empty the bladder with a catheter and give intramuscularly or preferably intravenously in the upper arm 6 mgr. of Phenolsulphonephthalein neutralised with Sodium Hydrate in 1 Cc. of water ('Sterules' of this strength are made.)

The urine is collected in test tubes containing a few drops of Liquor Potassæ. Normally the red colour appears in 5 to 10 mins., is at its maximum in 15 to 20 mins. and all the dye is excreted in 4 hours. There is reason to suspect deranged function when any of these times are increased.

Rowntree and Geraghty think that investigations on the lines of Urea output, total Nitrogen value, etc., are of no value.

In severe, acute nephritis the permeability is markedly decreased, also in chronic interstitial nephritis. The delayed appearance and especially the diminished excretion in the two hour period are more accurate indications of functional derangement than an estimation of total solids or Nitrogen.

In 18 clinically normal pregnancies there was a relatively diminished excretion (*i.e.*, interference with renal function) as compared with that in normal non-pregnant cases. The depression in Nitrogen secretion in late pregnancy may be due to interference in renal function and in absence of actual renal lesions the cause may be disturbed circulation due to pressure of the gravid uterus.—B.M.J.E. i./13,75.

Further report says, the rate of excretion is of less importance than the relative quantity excreted by each kidney and the fact whether the whole amount is excreted. The urinary pigment may be overcome by precipitating with Lead Acetate.—B.M.J.E., i./13,80.

Other observers require three hours as time. 60% should be excreted in this period.

The removal of blood and bile from the urine for the test by precipitation of hæmoglobin and bilirubin on addition of equal volume of saturated Alcoholic Zinc Acetate.—Jl.A.M.A. ii./25,1749.

In the stools of 9 out of 26 patients, after intravenous injection of 6 mgr., 1 to 8% of the amount injected was recovered, showing that the dye may be eliminated, resorbed, and transformed in the digestive tract. The duodenal tube, immediately after the injection, showed presence of 1 to 3% of the dye in the bile of three normals, while it was absent in the bile of 5 persons with liver disease.—Comptes Rend., per Jl.A.M.A. ii./25,309.

By tests on normals in which the urine was collected at 15-minute intervals for two hours, the curve of dye elimination by the kidneys was shown to be 40% during the first 15-minute period, 17% during the second, 8% during the third, and 4% during the fourth, gradually decreasing to 0.5% during the eighth. A series of cases of known renal insufficiency showed abnormalities in the curve, the presence of an abnormal curve indicating impending renal failure, while the other tests were negative.—Jl. Urology, per Jl.A.M.A. ii./25, 469.

In normal kidneys the colour appears in 5 to 10 minutes and the maximum colour in 15 to 20 minutes, while the total excretion should be complete in 4 hours.—G. A. Harrison, L. ii./28,1144.

TRENCH NEPHRITIS. A. G. Auld (B.M.J. ii./17,414) in an investigation of the urine by means of the dye considers that the first hour's reading is sufficient.

Special Committee on Renal Function. Report. Urea Concentration Test, Standard Method, Blood Urea Test, Diastase Test, Phenol Dye and Indigo-Carmine Tests.—L. ii./22,71.

Creatinine has been found an excellent substance as a test for renal function. As a result of experiments it was concluded that in normal persons and those with no real lesions the intravenous injection of 0.5 Gm. of Creatinine is followed by increased excretion. In chronic nephritis the increase is either nil or under 50%. It should serve as a useful confirmation of other methods.—R. H. Major, per Pres., April, '23,160.

The following is critical:

Phenolsulphonephthalein test of no prognostic value. Urea Concentration Test—results misleading, unless taken in conjunction with urea-content of blood. Urea-content of blood no guide to prognosis, nor commensurate with severity of symptoms. In general, the tests do not give any more definite evidence of severity of disease, or of probable outcome. They do not give any help in distinguishing between acute, sub-acute and chronic cases, and during disease merely corroborate clinical symptoms.—E. Crawford, L. i./24,78.

Phenolsulphonephthalein Test for Hydrocephalus.

Puncture one or other lateral ventricle and withdraw 1 or 2 Cc. of cerebrospinal fluid into a syringe containing 1 Cc. Phenolsulphonephthalein solution as used for Kidney Test. Inject mixture into ventricle and withdraw needle. After an interval perform lumbar puncture and allow spinal fluid to pass into a test-tube containing a few drops of 25% Sodium Hydrate solution: repeat in 30 minutes. Recovery of indicator (pink coloration of spinal fluid on contact with Sodium Hydrate) shows existence of hydrocephalus not due to intra-ventricular obstruction up to and including point of exit of the fluid from the fourth ventricle, i.e., it shows an extra-ventricular hydrocephalus: non-recovery of indicator shows intra-ventricular hydrocephalus.

Another test not so frequently used is the recovery of the ventricular injection substance from the urine. If ventricular hydrocephalus exists none of the indicator is recoverable within 2 hours: if an extra-ventricular hydrocephalus is present the indicator will be recoverable, but not as in a normal case. Technique more difficult and knowledge afforded similar to that of the simpler method.—Fraser's 'Surgery of Childhood,' 1926, p. 496.

Phenacetinum.

Manufacture.—For notes on the process of manufacture of Phenacetin, whereby one molecule of para-nitrophenol is made to yield a large number of Phenacetin molecules, *vide* May.

The action of Aniline and Paraminophenol derivatives is within limits proportional to the amount of Aniline, Paraminophenol or Phenetidine formed in the organism. Several more soluble derivatives of Phenacetin have been made, *e.g.*, by introducing Sulphonic for Carboxylic radicals, but these only tend to spoil the physiological action.—May, *cf.* also Lactyl-Phenetidine—the Lactyl analogue of the body under consideration.

The introduction of the acetyl group diminishes the formation of Phenetidin Hydrochloride, which is a poisonous body, in the stomach.—J. M. Fortescue-Brickdale.

A cold saturated solution treated with bromine water added drop by drop until the solution is permanently yellow should not become turbid (absence of acetanilide B.P. & U.S.).

☞ P1 COCÆ FOLIA.

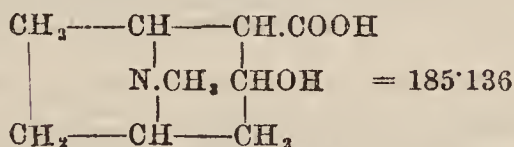
See also Vol., I. p. 331.

The leaves from BOLIVIA, PERU AND CEYLON contain Cocaine as their chief alkaloid, while the JAVA leaf contains chiefly Cinnamylcocaine, but little or no Cocaine, chemical treatment being necessary to convert the alkaloids into Cocaine. The genus *Erythroxylon*, which yields Cocaine alkaloids, comprises about 80 species, indigenous in 4 continents, of which only 4 or 5 have so far been completely examined as regards alkaloidal contents. The commercial supply comes from at least three distinct species. Suggested control of Cocaine traffic by restricted production of Coca leaves may prove more difficult than expected.—“Plant Alkaloids,” T. A. Henry, Review B.M.J. ii./24,626.

Assay.—Our examination of commercial samples of Coca leaves showed Ether-soluble alkaloids varying from 0.51-1.10% by titration and from 0.38 to 1.10% by weight. The highest average percentage of Ether-soluble alkaloid was obtained from small yellowish leaves, whilst the lowest average was given by large leaves; the former resembled Peruvian and the latter Bolivian Coca.

☞ P1 COCAINA.

Constitutionally, Cocaine is Ecgonine:—



with the hydrogen atoms in the carboxyl and hydroxyl groups replaced by a methyl and benzoyl group respectively.

For further details consult Gordon Sharp.—P.J. i./09,184.—‘Coca and Cocaine studied historically.’—*Vide also ibid.*, p. 356 for the synthesis of the racemic modification corresponding—physiologically and chemically—to natural cocaine by Willstätter.

There is **no local anæsthetic quite as good as Cocaine.**—M.P.C., Sept. 27/22,258.

The physiological activity of Cocaine is connected with the presence of the acylated hydroxyl group in the γ position with regard to the Nitrogen atom in the ring. Synthetic proof.—Ann. Rep. Chem. Soc., 1919 (Vol. XV.), p. 110.

Toxicology.—Cocaine is converted into ecgonine in the organism. Methods of detection.—Y.B.P., 1902,60.

A Cocaine Salt in solution may be estimated by precipitating Cocaine periodide with decinormal Iodine.—P.J. i./01,553,602; ii./01,223,254.

PERMANGANATE TEST FOR COCAINE AND OTHER BODIES. When a drop of a Solution of Cocaine is placed on a dried film formed by a Solution of Potassium Permanganate on a micro slide and examined under the microscope, oily drops are seen. If, however, the Cocaine is dissolved in a Saturated Solution of Alum, violet crystals of Cocaine Permanganate will be quickly observed. Atypin, Tropacocaine and Scopolamine produce crystals from Aqueous Solutions. Beta-Eucaine, Stovaine, Novocain and Holocain form no crystals with Permanganate. Saporette's Bromine Test distinguishes.—P.J. i./11, 94.

REICHARD'S TEST consists in adding a concentrated solution of Sodium Nitro-prusside, drop by drop, to a Cocaine salt solution containing at least 0.004 Gm. Cocaine per Cc. A precipitate of reddish crystals is formed which dissolves on warming and reappears after the liquid is cooled.

PISANI'S TEST. A wine-red colour is obtained by heating together Cocaine or Cocaine Hydrochloride with a few drops of Concentrated Sulphuric Acid containing 2% Formamide. The colour soon disappears, giving place to a brownish-grey precipitate. The test is stated to detect 0.001 Gm. Cocaine.

—Autenreith, Detection of Poisons and Powerful Drugs.
With Chromic Acid and Cobalt Nitrate Atypin behaves similar to Cocaine and Eucaine and precipitates with usual alkaloidal reagents and caustic and carbonated fixed alkalis and with ammonia.

The four alkaloids Cocaine, Truxilline $C_{13}H_{23}NO_4$ (previously called Cocamine or Isatropylcocaine), Cinnamyl-cocaine and Tropa-cocaine $C_8H_{14}NO.C_6H_5CO$, are known to exist in coca leaves.

A volumetric method for the estimation of Cocaine and Atropine in B.P. ointments.—H. J. Foster, B.P. Conf., 1921.

NOVOCAINE AND STOVAINE used as **adulterants** of Cocaine in Belgium. Methods of identification.—Y.B.P., 1922, 8.

VITALI'S REACTION.—Cocaine reaction similar to Atropine if the Alkaloidal residue, after mixing with Alcoholic solution of Potassium Hydroxide, is heated on water-bath, but gives no reaction in the cold—the reaction in this case, however, is found to be due to isatropyl-Cocaine as impurity.—Y.B.P., 1922, 7. Further experiments to show that the color is due to esters of the tropic acid series.—Y.B.P., '23, 24.

Extraction of (Crude) Cocaine is in the following stages:—

Treatment with (1) Sulphuric Acid 0.5%, (2) the liquor is rendered alkaline with Sodium Carbonate, avoiding excess, (3) stirring with Petroleum for 3 or 4 hours, (4) Extraction of the solvent with Acid 0.3%, then this with required amount of alkali. Collect and wash. The pasty mass contains 87 to 93% pure Cocaine.—O. Sperber, Tropenpflanzer, 1911, 15, 684—687, per J.S.C.I.

Purification of Crude Cocaine.

Cocaine, truxilline and cinnamyl-cocaine being ecgonine derivatives yield ecgonine, acids, and methyl alcohol on hydrolysis. This fact is of importance commercially as the amorphous residue remaining after extracting as much as possible of the crystalline cocaine can be converted into **ecgonine**, and this by treatment with benzoic anhydride and methyl alcohol can be converted synthetically into cocaine.

Although formerly care was taken in the extraction to preserve the Cocaine, now-a-days manufacturers rely on the ecgonine content. After isolation in the crude the 'Cocaine' is treated so to reintroduce the methyl and benzoyl group. Process for ecgonine estimation has been devised.—Am. Jl. Ph. Feb. '08, p. 74.

Cocaine volatilises at 100° C. This is of importance to recollect in analytical work.—Am. Jl. Ph., Dec. 1910, p. 576.

Beta-Naphthalene Sulphonic Acid used for purifying crude Cocaine. Crude Cocaine 10 Gm. is dissolved in hot water containing 5 Gm. of the acid and the solution filtered warm. On cooling, an oily resinous body deposits which becomes semi-crystalline. Ammonium Carbonate is added, then a solution of Ammonia which produces a white precipitate. This is extracted with Ether and the pure Cocaine crystallises out from the Ethereal solution. The acid used may be recovered by concentrating the mother liquors and precipitating with Hydrochloric Acid.

Another method is to dissolve crude Cocaine in boiling water containing Acetic Acid. On cooling, precipitate with Ammonium Carbonate yielding a resinous yellow precipitate lighter than water. The solution is filtered and Ammonia added. The Cocaine is crystallised from Ether.

The **ecgonine** contained in the resinous precipitate can be worked up. The residue is purified by crystallisation from Alcohol and pure Ecgonine precipitated by Sodium Carbonate. It is dissolved in Methyl Alcohol and the solution treated with anhydrous Hydrochloric Acid. Of the Methyl Ecgonine obtained 20 Gm. is heated on a water bath with Benzoyl Chloride 20 Gm. until no more Hydrochloric Acid is evolved. The solution is added to cold water. Benzoic Acid is precipitated. This is filtered out and the filtrate concentrated. The Synthetic Cocaine (termed **Coca-Ethylene** in the German Patent 47,713) is then precipitated from the filtrate by means of ammonia.—De Rosemont, *Jl. Suisse de Pharm.*, Apl. 29/20, abst. C.D. '20,934.

Cocainæ Hydrochloridum. *See also Vol. I., p. 336.*

It should not only be in good crystals, but should, by the following modification of **MacLagan's Test**, yield a distinctly crystalline precipitate of pure Cocaine within three minutes when 1 grain of it is dissolved in 2 ounces of distilled water, and six to eight drops of solution of ammonia, B.P., are added and well stirred. If more than 4% of amorphous alkaloid (principally Truxilline) be present, there will be only a cloudiness. The precipitate re-dissolves after twenty-four hours or more, the Cocaine being converted into methyl alcohol and benzoyl-ecgonine. Truxilline is highly toxic. (Fr. Cx. also gives this test and states the same. P.G.VI. gives it in a modified form.)

M.pt. should be taken by placing the tube in a bath previously heated to 195° C., when the M.pt. should not be below 197° C. The *melting point of the salt given in pharmacopœias is too low for the salt as prepared at the present time.*—Wilfred Smith, *P.J.* ii./28,88.

Sterilisation of Cocaine Hydrochloride Solutions.

Definite evidence, at any rate with 2% solution in ophthalmic work (*See Edn. XVIII., Vol. II., p. 63*), shows that boiling is safe.

Cocaine Hydrochloride is sterilisable at 115° C. for 15 to 20 minutes in the autoclave. A useful list of various temperatures for drugs.—*P.J.* i./19,34.

Efficiency of Cocaine Solutions is **not impaired** by boiling.—*Rep. Com. Local Anæsthetics*.—*Chem. Absts.*, 1922.

Drug Addiction.

In U.S.A. Drug addicts said to number 175,000. 90% of Opium and Cocaine entering U.S.A. said to be for other than legitimate medicinal purposes. Prohibition something to do with it.—W. E. Dixon, *B.M.J.* ii./21,822. *See also a further Abstract of this paper under Morphine, Vol. I., p. 567.*

“**BILLIE CARLTON**” CASE. Death from overdose of Cocaine self-administered—unlawfully supplied to her by De Veuille in a culpable negligent manner. Other cases of sale contrary to regulations.—*C.D.*, Feb. 1/19, p. 93, 245.

PERFORATION OF NASAL SEPTUM in Cocaine snufflers. Cocaine habit alarming at Geneva.—F. G. Crookshank, *B.M.J.* ii./21,917.

Unfounded suspicion should not enter into the matter.—H. Tilley, *B.M.J.* ii./21,1008. Harmless nasal affection not to be confused.—J. F. O'Malley, *B.M.J.* ii./21,1008. The perforation is always *circular*, not button hole.—F. G. Crookshank, *ibid.*, 1055.

Cocaine abuse leads to rapid degeneration, morally, mentally and physically. Smuggled mostly from Germany. Mild Cocaine poisoning produces a feeling of general well being (euphoria). It is stated that Cocaine even in therapeutic doses may produce sexual excitement and, so far as reported cases go, appears chiefly in women— from which fact arises the danger for dentists! It is admitted the effects are only occasionally seen or heard of.—*B.M.J.* i./22,849. We have *never* heard from dentists, of the danger.

Alcoholism and drug habit. The late Oscar Jennings made a statement that one in four medical practitioners took drugs. Of twelve varied cases under treatment six were doctors.—Stanford Park, *M.P.C.*, Jan. 24/23,74.

Trade in Dangerous Drugs.—Figures showing quantities of Morphine Heroin, and salts, manufactured and exported in the years 1910-1923.—*L.* ii./24,921.

Drugs of addiction must be withheld from sufferers from mental depression. Focal sepsis, *e.g.*, dental trouble, may lead to Alcohol and Morphine addiction. Opium *per os*, in small amounts, becomes a necessary routine amongst natives

in Eastern countries. In the Fen counties here Laudanum and Opium addiction was not uncommon at one time—possibly from taking the drug to counteract the effects of malaria, which was prevalent in those days. Association with addicts is one of the commonest causes of addiction. Morphine and its derivatives appear to have a *sedative effect* on sexual impulses, and to lead to impotence and sterility. These are often taken by those sexually vicious to stifle the calls of conscience. **Withdrawal symptoms**, in the case of a child born of a woman who had had 4 to 6 grains of Morphine a day during her pregnancy, are described. These were overcome during the first few days of its life by small doses of Tinct. Camph. Co. Some hold that an antidotal substance is formed in the body of an addict, which neutralises the large amounts of drug taken. Probably definite **degenerative changes** occur in the nerve cells of the brain, and this leads to abnormal channels of transmission of nerve impulses, producing abnormal physical and mental effects. Where general health is good, there is no harm in prompt, complete withdrawal. Where it is poor, **Hyoscine** hypodermically has been advised. The International Opium Convention at the Hague, 1912, ultimately gave birth to the D.D.A.'s. Loyal co-operation of the professions enjoined.—Sir W. H. Willcox, B.M.J. ii./23, 1015; P.J. i./24, 14, 27.

The public ought not to be deprived of commodities or services because of possible abuse of them by invincibly ignorant, incurably stupid, culpably careless or evilly disposed persons.—P.J. ii./24, 332.

Harrison Federal Law in U.S.A. applies (1) to preparations containing more than 2 grains of Opium, $\frac{1}{4}$ grain of Morphine, $\frac{1}{8}$ grain Heroin, 1 grain of Codeine, or any salt or derivative of them in 1 fl. oz. (2) or to liniments, ointments, or other preparations containing Cocaine or any salt, or α or β Eucaine, or any of their salts, or any synthetic substitute for them. There is *no minimum limit* to Cocaine.—P.J. i./24, 181. Cf. also recent inclusion of **Heroin in any proportion** under the 1925 Dangerous Drugs Act—the result of International Conference.

In New York out of 7,464 cases 96.5% were found to be Heroin addicts, while in Chicago less than 4% of addicts use this narcotic. Paregoric habitués are fairly common, some taking as much as a quart a day. The number of those who patronise illicit narcotic street vendors in New York City is not less than 10,000.—M.P.C., April 2/24, 268.

Dangerous Drugs Acts.

There were 60 prosecutions under the Acts in 1927, and 50 convictions. 65,746 ounces of Morphine were used in this country for the manufacture of Codeine. The amount of British Morphine manufactured and imported continues to fall, the amount exported in 1927 being 66,107 oz. as against 14 tons a few years ago, but there is an increase in Heroin—17,427 oz. manufactured as against 11,113 oz. in 1926.—L. ii./28, 236.

Successful Appeal by a Liverpool chemist against a conviction for unlawfully dispensing a prescription for 20 grs. Morphine Sulphate without having taken reasonably sufficient steps to see that the prescription was genuine. The prescriber had practised as a doctor in Canada, but had lost his qualifications and been deported—he had also posed as a doctor in Liverpool and had attended patients. The prescriber was convicted and sentenced to imprisonment. A doctor who had met the prescriber stated that the more a chemist had examined him the more he would have been satisfied that the prescriber was a doctor. The Recorder said that if there was nothing to make a doctor suspicious there was **nothing to make the chemist suspicious**, and the latter's appeal was allowed with costs.

A chemist who gradually becomes acquainted with the signatures of doctors practising in his neighbourhood can hardly be expected to go through a similar process when presented with a prescription over a signature with which he is unfamiliar. **Is it to be deemed compulsory for a chemist to keep on his premises a copy of the latest medical list?** Even if he does, he may **still be deceived** by a **forged signature**, or the doctor may have lost his qualifications since the list was published.—L. ii./28, 353.

British Report on Dangerous Drugs to the League of Nations for 1927.—C.D. ii./28, 62.

COCAINE SUBSTITUTES.*See also Vol. I., p. 343, et seq.*

Stovaine Identification, e.g., in Liquor Cerebralis and Urine after spinal anæsthesia. Extraction with Ether and thence into dilute HCl. Iodine will show 1 in 150,000.

Novocain, Identification.—To a 0.2% solution add 2 drops of 10% Sodium Nitrite and 3 drops Sulphuric Acid and heat; then dilute with water and treat with Millon's Reagent. Red colour—identifies the Phenolic Nucleus. The Ethyl is identified by the formation of Iodoform and the Aldehyde by distilling the substance with dilute Sulphuric Acid and Manganese Dioxide and testing the filtrate with Magenta—Sulphurous Acid reagent. Bromine gives a yellow precipitate with Novocain Solution which dissolves on warming.

On mixing solutions of Novocain, Sodium Nitrite, Hydrochloric Acid and Sodium Carbonate containing 0.5% of Potassium Guaiacol-sulphonate, a color varying from red to yellow according to dilution, is formed, which can be used for colorimetric estimation, using a 1 in 20,000 solution as control. Reaction not given by Methyl *m*-amino *p*-hydroxybenzoate, *p*-amino-benzoic Acid, Cocaine, or Stovaine.—J.C.S., A. ii./25,247.

Solutions of Novocain may be sterilised in slightly alkaline glass vessels at 100° without change, but at 120° the alkali causes appreciable change.—J.C.S., A. ii./25,247.

Pharmacology of Local Anæsthetics (Cocaine and substitutes).

Eggleston & Hatcher, *Jl. Pharm. and Exp. Therap.*, Vol. XIII., 1919, found that "five, or more than five, times the minimal fatal vein dose of Alypin, beta-eucaine, stovaine and tropacocaine can be injected subcutaneously in the cat without causing death, while four, or less than four, times the fatal vein doses of cocaine and holocaine similarly injected prove fatal"; further, that "the simultaneous subcutaneous injection of adrenalin with the local anæsthetics reduces the toxicity of the latter by delaying absorption rate, but this reduction is much less marked in the cases of cocaine and holocaine than with the other members of the series, and is referable to their much slower 'essential' elimination."

A committee appointed by the American Medical Association to study the occurrence of accidents arising from the use of local anæsthetics reported 43 unpublished deaths, of which Cocaine was responsible for 23. Novocain was found to be the most frequently employed and by far the safest. Butyn, Cocaine, Alypin, Apothetin and Stovaine are probably equally dangerous when injected into the tissues. Committee advises that Cocaine should not be given hypodermically, neither should concentrated solutions be applied to mucous membranes. Not more than 15 minims of 10% Cocaine should be applied to the throat or nose and not more than 1.5 grains given when applied to a mucous membrane—urethral injections especially dangerous. Novocain should not be injected in concentrations above 1%, and Butyn should not be injected but may be applied in a 2% solution.—B.M.J. i./24,871.

Novocain (German) and the corresponding products, Neocaine (French) and Procaine (American), have equal toxicity and are equally effective. Apothetine (American) is more toxic.—W. R. Meeker and E. B. Frazer, *Jl. Pharm. Exp. Ther.*, '24, 22,375, per J.C.S., A. i./24,1377.

Isocaine (*p*-Amino-benzoyldi-isopropyl-aminoethanol) has approximately the same efficiency as Cocaine in anæsthetising the cornea, and only three tenths of its toxicity. It is twice as toxic as Procaine, and hence less suitable for paralysis of sensory nerve trunks, although equally efficient.

COLCHICUM.*See also Vol. I., p. 357.*

The corms are usually weaker in alkaloid than the seeds; about 0.3 to 0.8% is found in both. Acetic Acid is nearly equal to Proof Spirit to extract Corm and Seed.

Assay of Colchicum by Phospho-tungstic Acid.—E. C. Davies, P.J. i./21,505. Iodine may also be employed as precipitant.

Estimation by shaking out the alkaloid with Chloroform and then precipitating with Phospho-Tungstic Acid (Scheibler's Reagent). Precautions necessary in estimating Colchicine due to the presence of an amino-acid grouping.—J. Grier, P.J. ii./23,87.

CONIUM.

See also Vol. I., p. 381.

The amount of alkaloid found in the root, stem, and leaves is small, while in the fruit it is considerable during the period when the fruit is forming its reserve material, reaching as much as 3 per cent. or even more. When the fruit has finished forming its reserve and ripens, the proportion of alkaloid is found to become less, not greater, until it falls to less than 1 per cent. in the ripe fruit. Moreover, the proportion of alkaloid to total nitrogen gradually diminishes as the fruit develops. If the alkaloid were a by-product, as viewed by Pictet, in the production of protein it might be expected to retain a fairly constant ratio, and not become a diminishing one.—E. H. Farr, Pres. Add. B.P. Conf., 1914, P.J. ii./14,117.

The U.S. VIII. ASSAY METHOD is unsatisfactory. That in the 1901 "B.P.C. Formulary" is better. (Conium is no longer official in the U.S.P.).

There is no 'dry' reaction characteristic of Conine.

A scheme for differentiating Conine, Nicotine, Lobeline, Sparteine, the Conhydrines, Coniceine, and a new isomer is given.—P.J. ii./09,103; see also P.J.ii./05,333; see also P.J. ii./09,70, *et seq.*

CREOSOTUM (B.P. '14).

See also Vol. I., p. 383.

Ⓟ **Creosote.** According to FR. CX. consists of about half its bulk Creosol, the other half consisting of Guaiacol with some cresylols, phlorol, or orthoethylphenol, etc. Soluble readily in alcohol, ether, anhydrous glycerin, chloroform, also in caustic potash and soda solutions, and in acetic acid (glacial). It distils between 200 and 220° C.

B.P. '14. Sp. Gr. not below 1.080. (P.G. VI., 1.075).

Genuine Beechwood Creosote yielded 39% Monophenols, 26.48% Guaiacol, 32.14% Creosol $C_6H_5CH_2.OCH_3.OH$ and homologues, Pinewood Creosote about the same but 20.3% Guaiacol and 37.5% Creosol and homologues—all boiling between 200 and 210° C.

Creosote is usually optically inactive but may be slightly dextrorotatory.

Potassium Guaiacol Sulphonate.—Incinerate 0.2 Gm. until the residue is white. Cool, and incinerate again after adding a few drops of concentrated Sulphuric Acid. Renew this until weight is constant. Weight of residue should not be less than 0.064 Gm. nor more than 0.072 Gm. The aqueous solution 1 : 20 should not become turbid on the addition of sulphuric acid.

Arsinic Acid Derivatives of Guaiacol.—R. G. Fargher, J.C.S., July, '20, 865.

CUPRUM.

Kraemer suggested that strips of copper foil kept in drinking water jugs would kill *B. Coli* and *B. Typhosus*. We tried this recently (1929) and found the method inefficient. *See Water Analysis.*

Various foodstuffs, milk, fish, eggs, etc., contain small amounts of copper.

Copper for water service pipes.—L. i./25,1357.

Belladonna and Henbane have been found to contain small amounts.

Copper determination in foodstuffs colorimetrically by Ferrocyanide and gravimetrically by precipitation with Quinosol.—Analyst, '26,327.

To kill Algae in Ponds, etc.

It is stated that, without injury to plants or fish, Copper Sulphate not exceeding 2½ ounces per 10,000 gallons can be employed. The crystals should be slightly crushed and placed in a coarse bag and drawn to and fro across the pond. To estimate the amount of water in the pond take the average breadth and length and multiply them together and the result by the average depth, all expressed in feet. Then multiply this by 6½ and the result will give the number of gallons. If the first application does not suffice, repeat in a week or ten days.

Organic Copper Compounds.

Cupri Alloxanas ($\text{N}_2\text{C}_4\text{O}_4\text{H}$)₂ Cu.

A bluish green flocculent powder slightly soluble in water. The relative insolubility is a disadvantage from the therapeutic standpoint.

Cupri Glycinas ($\text{NH}_2\text{CH}_2\text{COO}$)₂ Cu.

A blue flocculent silky powder soluble about 1 in 200 of water at 15° C., but more than twice as soluble at 40° C.

0.06 Gm. per kilo in 0.5% solution intravenously killed a rabbit in 8 minutes, whilst a control of Salvarsan in proportion 0.1 Gm. per kilo was tolerated, hence the substance has a toxic dose of about 2 Gm. for an average man.

Cupri Hippuras ($\text{C}_6\text{H}_5\text{CO.NHCH}_2\text{COO}$)₂ Cu.

A bluish green crystalline powder. Almost insoluble in water, but soluble about 1 in 200 of a mixture of glycerin and water equal parts. It is more soluble in pure glycerin.—Suggested by G. T. Morgan.

Rats maintained for 2 or 3 months on diets containing a high proportion of peas to which copper was added grew normally and did not suffer in health. Most of the copper is excreted by the alimentary tract; a small proportion may be absorbed in the blood, retained in part for a time by the liver and then excreted by the kidneys.—B.M.J. i./24,680.

DIGITALIS FOLIA.

See also Vol. I., p. 392.

Preservation.—The dried leaves should be kept in small containers over a layer of lime,—the freshly burnt quicklime being in a wide mouth bottle tied over with a layer of gauze. The freshly powdered leaf is favoured by many as the best method of giving the drug.

F. Norsk. advises leaves of the indigenous wild-growing flowering plant dried for five hours at about 80° C., filled into well-closed containers of not more than 50 Gm. The same rule applies to powdered Digitalis.

Deterioration of Preparations of Digitalis we deal with under ASSAY.

Cultivation.—

We are of the opinion that a **dry season favours potency**. The most potent leaves that we have examined (both chemically and physiologically) were second year's leaves from plants grown in England in a **sunny exposed situation**. These leaves were from plants showing no flower spikes at time of collection. (NOTE.—*All second year's plants do not necessarily flower.* We lay more stress on the sunny situation than the point of non-flowering at the time). Ransom and Henderson found sunlight to influence the alkaloidal content of Belladonna which resembles Digitalis in nature in being a plant growing in semi-shade.

The petioles and midribs of the leaves contain less of the active principles than the lamina—they can be removed by sifting. *Heavy* seed should be used for cultivation.

In New Zealand Digitalis has become a noxious weed, as also *Hypericum Perforatum*.—P.J. i./20,522.

D. gloxiniflora (a gloxinia-like strain) leaves approximate *D. purpurea* in potency.

D. ambigua from Austria, and *D. lutea* from America, as good therapeutically as *D. purpurea*. Digitalis leaf of good quality grown in the valley of Kashmir and at Mungpoo (Eastern Himalayas).—R. N. Chopra, I.M.G., Mar., '26, 117; *ibid* May, '26, 212.

First or second year's leaves the best?

Second year's leaves have been found stronger than the first, *i.e.*, in proportion of 10 to 8½—but some disagree with this.

Fockes says that second year's leaves have their highest value while flowering, and the first year's leaves attached to them the highest value in late summer.

We think there is little to choose between them. *A dry season will produce less yield of herb than a wet one, but an increased proportion of active glucosides.*

Though the *B.P.* directs the leaves to be collected at the time of flowering, *i.e.*, in June or July (second year's growth) a good tincture can be made from leaves collected as late as end of September.

Most toxic extract obtained by gathering leaves *in the afternoon* and immediately plunging into 96% Alcohol.—*J.C.S.A.* i./22,97.

Gordon Sharp and F. W. Branson found that leaves gathered in November are as active as those gathered in August, and that leaves from plants that had flowered are equally as toxic as those from plants that had not yet flowered.

Content of Active Constituents.—

The content in the leaf of Digitoxin is about 0.1 to 0.4%. The average dose of this is 0.5 mgr., corresponding to the effects of 0.06 Gm. of *Digitalis* leaves—but this quantity of leaf would contain only 0.12 mgr., so there is a discrepancy of about 400%. **Digitoxin therefore represents only about $\frac{1}{4}$ the power of *Digitalis*.** To assay *Digitalis* by Digitoxin alone would be about as rational as to assay Opium by Codeine content. The Leaf Margin (epidermis and endodermis) gives the strongest micro-chemical reaction for glucoside content, the base of the petiole only a very faint one.

Tincture of *Digitalis*.—'Abel Scholar' found that cold water extracts most of the soluble constituents of those removed by the official alcohol strength.

All the active water-soluble principles of *Digitalis* leaves are extracted in making Tinct. *Digitalis*. An infusion can be made to keep good for two years.—Weiss & Hatcher, *J.A.M.A.*, Feb. 19/21, per *B.M.J.E.* i./21,61. *cf.* *Liq. Digitalis ad Injectionem*, *Ph. Ned. V.*, our Vol. I., 396, which is an *aqueous* extractive.

Fresh concentrated infusions made with 20% Alcohol or 0.1% Chloroform Water are essentially Digitoxin preparations, whereas *the fresh B.P. infusion is a Digitalein preparation*. Old concentrated infusions showed absence of therapeutic value in the filtrate with presence of toxic effects, the sediment being also toxic and possessing tonic effect.—K. Samaani, *P.J.* i./21,481.

Acetone extracts the whole of the principles of *Digitalis* called Pandigitonin.—A. Tschirch. Schweiz. Ap. Zeit, Y.B.P., 1919,84.

Ether is first used to free from resins, fat, etc., the glucosides being insoluble in Ether.—C.D., '20,1372.

***Digitalis* Bodies.** Further work on.—Digitogenic Acid, Digitaligenin, Digitoxigenin.—H. Kiliani, *J.C.S.A.*, i./20,320.

Extraction of active principles of *Digitalis*.—E. Mameli, *Chem. Abstr.* 1922,4011, Y.B.P., '23,140.

Characters and Tests of Glucosides.

The determination of the value of a *Digitalis* preparation (especially the Tincture) by chemical means is fraught with considerable difficulties owing to many factors, *e.g.*, the numerous glucosidal bodies contained, the fact that it is not possible to point to one glucoside as the potent constituent as representing the activity of the drug, and again the extraction of the substance in any degree of purity requires some analytical skill.

We adopted as our standard a Tincture having by physiological tests a M.L.D. calculated as 0.75 Cc. per 100 Gm. weight of frog.

In a paper read before the Pharmaceutical Society of Great Britain, Dec. 10/1912, the results of examination were provided of a number of samples of leaves both of the author's growing and from sources in various parts of the world (Great Britain, Germany, Italy, India, etc.). Almost all of these leaves gave tinctures of Standard or above Standard strength. The paper was published in booklet form entitled '*Digitalis* Assay.'

The glucosidal bodies with which we are concerned are :—

From *Digitalis* Leaves.

Digitoxin the most potent glucoside present.

GITALIN which is the name given by Kraft to DIGITALEIN of Schmiedeberg and Kiliani in a purified form. **DIGITONIN AMORPH.** *Syn.* DIGITSAPONIN Kraft. **GITIN.**—A further Saponin. The last two are relatively inactive.

The **Colorimetric Method** devised gives results equivalent to the Physiological Assay Method based on the minimum lethal dose required to kill a frog and calculated to 100 Gm. body weight. The method requires some care in carrying out, as it is strictly quantitative. It is as follows :—

To determine whether a Tincture is up to Physiological Test requirements (usually taken at M.L.D. = 0.75 Cc. per 100 Gm. body weight of frog) mix 10 Cc. of the Tincture with 16 Cc. of water, precipitate with 10% Neutral Lead Acetate Solution (about 3 Cc.), adding a little Kieselguhr. Allow to stand for a $\frac{1}{4}$ hour, filter off on the pump, wash the precipitate slightly. Remove excess of lead from the filtrate with 10% Sodium Phosphate Solution (about 2 Cc. required) and filter. Add a little Calcium Carbonate (about 0.2 Gm.) to the filtrate (to prevent possible hydrolysis of the glucosides), and evaporate to dryness on a water-bath. Add about 2 Gm. of dry washed sand to the residue and extract with Chloroform five times by thorough trituration using about 10 Cc. on each occasion. Filter and evaporate the Chloroformic Solution and extract the residue with warm water on the water-bath, using 10 Cc. and 5 Cc. and again employing sand. Filter, evaporate to dryness in a porcelain basin, extract the residue again with cold Chloroform to purify it (about three or four quantities of 5 Cc. each using dry sand and triturating thoroughly with a small pestle) and filter. Evaporate the combined Chloroformic Liquors and dissolve the residue in 4 Cc. of Glacial Acetic Acid. Mix 0.1 Cc. of this Acetic Solution with 1 Cc. of Sulphuric Ammonium Molybdate Reagent in a 5 × 1 Cm. test tube and compare the depth of colour after five minutes with the scale below—this coloration indicates the *content of combined "active water soluble" Glucosides* (probably including Digitoxin). Further, if 0.1 Cc. of the Acetic Solution be mixed with 0.5 Cc. of Glacial Acetic Acid, and this be layered upon 1 Cc. of the Sulphuric Ammonium Molybdate Reagent, the typical blue ring showing presence of Digitoxin should be formed.

SCALE.

BELOW
STANDARD.
No. 0.

STANDARD.

No. 1.

ABOVE STANDARD.

No. 2.

No. 3.



= M.L.D. of 0.9 Cc. = 0.75 Cc. = 0.6 to 0.5 Cc. = 0.4 to 0.3 Cc.

Mount the tubes on a little slab of Plasticine and observe the colours by direct transmitted light using a white background.

Face page 73, Vol. II.

E. Berry (P.J. ii./15,783) mentions also an irritating fat or resin soluble in ether, a fluorescent body LUTEOLIN or DIGITOFLLAVONE and an active enzyme oxidase.

From Digitalis Seeds.

Digitalin. (*Syn.* Digitalinum Verum).

DIGITALIN. Common to leaves and seeds *vide antea*.

DIGITONIN AMORPH. (Schmiedeberg) and **DIGITONIN CRYST.** of Killiani.

Digitoxin Recognition Tests.

Keller-Kiliani (*Syn.* Keller's Test) for Digitoxin in the Leaves.—Shake 10 Cc. of filtered infusion in boiling water 1+20 in a separator for a few minutes with chloroform 10 Cc., add ether 5 Cc. and alcohol 5 Cc.; shake again and filter off the chloroform-ether solution through a filter moistened with chloroform. The liquid is evaporated and the residue dissolved in 3 Cc. of acetic acid (96%). A drop of diluted solution of ferric chloride (1+19) is added, and the whole, in a narrow test-tube, is layered carefully upon sulphuric acid; at the point of contact of the two liquids a brownish-red zone develops, and over it a bluish-green zone.—P.G.V. We find in practice the presence of Chlorophyll hinders the coloration considerably.

The test may also be applied to the glucosidal substance *Digitoxin* thus:—Dissolve 0.001 Gm. in 3 Cc. Glacial Acetic Acid, add a few drops of the Ferric Chloride Solution and proceed exactly as the rest of the last mentioned.

Fröhde's Test (Sulphuric Ammonium Molybdate *vide* Colorimetric Method *infra*) Ammonium Molybdate 1% *w/v* in concentrated Sulphuric Acid used as a *mixing* test gives characteristic maroon colour with the water soluble glucosides—see colour scale. Used as a layering test, it gives a characteristic blue ring.

Kiliani Test for Digitalin.

Ferric Sulphate 0.05 Gm. is dissolved in water 1 Cc., and Sulphuric Acid added to 100 Cc. Employed as a mixing test (0.1 mgr. of the glucoside is sufficient, dissolved in 0.2 Cc. of Glacial Acetic Acid), this reagent produces pink coloration.

This test with *Digitoxin* produces a brownish colour.

Chemical Assay processes used in the past, centred on an estimation of the *Digitoxin*—*ignoring the bodies which are known to be readily soluble in water*. That this was fallacious was shown by Ziegenbein, who found that leaves containing only 0.125% of this glucoside were twice as active as those containing 0.226%.

Our aim was a method to include the latter in addition to Digitoxin or an allied body. The process effects this and includes a strong indication of Digitoxin—either through the actual solubility of it in the repeated quantities of solvent (the amount of Digitoxin in 10 Cc. of Tincture is extremely minute though sufficient to detect) or owing to the fact that Digitoxin is soluble in the presence of the other Glucosides and Saponins. Results approximating the physiological “M.L.D.” results were obtained with the samples of Tinctures referred to, even after 12 months' storage.

It was also possible to prove that a tincture kept 12 years under adverse conditions had an M.L.D. of 0.7 Cc.

The work has been spread over a period of years—since 1912, and we have since that date frequently compared our findings with Physiological reports and we know that it gives concordant results.

Tincture made from 1929 leaves of our own growing were found to be up to standard. (M. L. D. 0.75 Cc.)

D. Purpurea grown in the Nilgiris, Madras, India, was found well up to standard both by W. H. Martindale's Colour Test and Physiological Tests.—Gordon Sharp, P.J. ii./17,108.

E. Berry extended the author's process for estimation of Digitalis leaves and employing similar reagents estimates (A) the content of water-soluble glucosides only, (B) the content of total glucosides. In the latter Alcohol of 70% strength is maintained throughout to keep all the glucosides in solution. The result of (A) is called the Therapeutic Value.—B.P. Conf., 1919.

Tschirch confirms Ziegenbein that the Digitoxin content in *Digitalis* leaves is not in proportion to the physiological activity. It was found that *Chloroform must be used repeatedly* (eight shakings) to remove the entire active substances (we have found this also : note the *repeated extraction* in our colour method). **The active substances are in some form of combination which is broken up by the repeated shaking.** Absolute Alcohol, **Acetone** and Amyl Alcohol will exhaust leaves completely ; Chloroform, Acetic Ether and Benzene partially. Ether and Carbon Tetrachloride do not extract the active substances at all. Acetone is specially good as yielding a colourless extractive. It can be used for assaying. (The use of Acetone instead of Chloroform in our method would no doubt yield even more interesting results.)—Schweiz, Ap. Zeit., Vol. 56, p. 469, abst. P.J. i./19,219.

Physiological Standardisation.—

A. Goodall found of 23 tinctures examined (*laboratory samples, not those of commerce*), only 12 were up to the average, 6 were under; and instead of a maximum dose of 15 minims from 18 to 25 minims were necessary. Several were above strength, *e.g.*, 4 to 10 minims. End point employed was death in four hours. A standard preparation of Tincture *Digitalis* remains active twelve months.—B.M.J. ii./12,47,149.

Comparison of Physiological Standards.—The various workers on the subject—Cushny, Dixon, Houghton, Martin, etc., have from time to time set up the most divergent time limits for the death of the frog employed in the test. We went very fully into this matter in previous Editions.

Digitalis, Strophanthus and Squill in the U.S.X. are assayed by determining the systolic dose for frogs in comparison with Ouabain, *see* Vol. I. p. 396.

Owing to *seasonal variation* a standard of Ouabain was advised in U.S. IX. and corrections made if necessary.

The standards were as follows :—

	Gm. or Cc. for each Gm. of frog.		Gm. or Cc. for each Gm. of frog.
OUABAIN	0.0000005	STROPHANTHUS—	
DIGITALIS—		Seed (in form of tincture)	0.000006
Leaves (in form of tincture)	0.0006	Tincture	0.00006
Fluid Extract (not now in U.S.)	0.0006	SQUILL—	
Tincture	0.006	Dried (in tincture form)	0.0006
		Fluid Extract	0.0006
		Tincture	0.006

The *Ouabain method* is now recognised as unsound.

Pithing frogs prior to experiment is as followr :—The brain of the animal is destroyed from the nape of the neck upwards, i.e., the spinal cord is divided in the neck and then a wooden pointer is passed up into the brain (the centres of feeling), thus leaving the spinal cord intact and the heart untouched. A frog has been known to “live” for years with its brain destroyed. The animal feels nothing but its heart goes on beating and its reflex centres are alive.

Comparative standardisation of three samples of dried and powdered *Digitalis* of different activities carried out by a number of experts.—Med. Res. Council, P.J. i./25,78.

Discrepancies in assaying under Med. Res. Council (Cardio-graphic Dept., U. C. H. Med. School), B.M.J. i./22,74.

Digitalis Flowers. S. Hirohashi, Pharm. Soc. of Japan Journal, No. 369, states the *Digitalis* flowers probably contain more active principles than the leaves (? W. H. M.). He found that an absolute alcohol extract of flowers fourteen months old was stronger physiologically than a similar preparation of fresh leaves. So far as the activity of the fruit is concerned, he puts it at the same as the leaves, while the leaf-stalk is not so active as the leaves.

Digitalis Seeds are said to be ten times more toxic than the leaves.

The seeds contain very little Digitoxin, which is generally considered the most valuable constituent and a relatively large amount of Digitonin which has little or no use as a cardiac tonic.—Dixon, Q. Jl. Med., Jan., '12, 297.

We prepared a **Tincture of the Seeds**. Our physiologist reported as follows upon it. Tested on the excised frog's heart, it was found that after removal of the Digitonin in which it was rich, the seed preparation proved to be weaker than an ordinary Tincture. Hence as it seems to be therapeutically weaker and yet more toxic than Leaf Tincture, it does not appear to be a desirable preparation. Digitonin is considered to be irritant to the alimentary canal.

Recent Data on Biological Assay of Digitalis, etc.

International Standard Digitalis Powder.

The **League of Nations Commission** on the Standardisation of Serum, Serological Reactions and Biological Products recommended the following methods of testing as suitable: (a) The frog method in the form advised by the second Int. Geneva Conf., 1925. (b) The method of intravenous infusion in the mammal, as described by **Hatcher** and **modified by Magnus for the cat**, by Knaffl-Lenz for the guinea-pig, or Tiffeneau for the dog. Also recommended that when the dosage of Digitalis, or preparations, is expressed in units of activity, the unit employed should be an international unit, defined as the specific activity contained in 0.1 Gm. of the International Standard Powder.—B.M.J., ii./28, 111. The standardisation of Digitalis against **Ouabain is now recognised as unsound.**—*Ibid.*

The **fatal dose** of the Standard Powder (1926) obtained by mixing various samples was 89.7 mgr. per cat kilo, 1 Gm. containing 11.1 fatal cat doses.

For further details see *Arch. Exp. Pathol. u. Pharm.* 1926, Bd. 112, S. 252, and Bd. 113, S. 40.

Fourteen samples were found to conform with the requirements of the League of Nations Conference, 1925. The cat method used in comparison with the International Standard.—Ph. Soc. Pharmacol. Lab. Rep., P.J. i./27, 133.

See also A. McFarlane and G. A. Masson on standardisation by the Cat Unit method.—Jl. Ph. & Exp. Ther., Feb. '27, 293.

Physiologically Tested Tinct. Digitalis. Certificates give very varying strengths for preparations made strictly on *B.P.* lines—W. Wolstenholm P.J. i./28, 89. The Cat unit employed.—L.H. Matthews, P.J. i./28, 141.

A method of assay using *guinea-pigs* instead of cats. An exhaustive list of references to contributors to the study of Digitalis is given.—E. Knaffl-Lenz, Jl. Ph. & Exp. Ther., Oct. '26, 407.

Cat method of assay only approximately accurate as a measure of toxicity of the preparation (account must be taken of absorbability of the preparation from the alimentary canal), but probably fully as accurate as the official frog method.—C. C. Haskell, Jl. Pharm. & Exp. Therap., June '28, 216.

The potency of Digitalis, as judged by the cat method of assay, is not lowered by exposure either to ordinary or to polarised light.—W. R. Bond and E. W. Gray, Jl. Pharm. & Exp. Therap., Mar. '28, 358.

Tinctures of Squills assayed in terms of Ouabain by the cat method gave results differing from those obtained by the frog method and although their assay in terms of Scillaren agreed it has been found advisable to compare tinctures sent to be tested with a standard composite Tincture of Squill, such a tincture being prepared by mixing about 9 tinctures made from a collection of samples of Squill obtained annually. A 25% variation is allowed. 100 Cc. of this tincture are equivalent to 0.0258 Gm. Scillaren.—J. H. Burn, Pharm. Lab., Ph. Soc., P.J. i./27, 328.

A clinical standardisation of Digitalis.—L. E. Martin, Jl. Ph. Exp. Ther. July '27, 229.

TABLE OF THE COMMON ENZYMES AND FERMENTS.

ENZYME OR FERMENT.	CHIEF SOURCE.	SUBSTRATE AND PRODUCT(S).
Amylase and Diastase	Human saliva, Malt and pancreas.	Hydrolyses starch, forming dextrin and Maltose.
Catalase (<i>see also Peroxidase</i>)	Blood, most animal and plant juices.	Decomposes Hydrogen Peroxide and other Peroxides.
Cellulase	Grass eating animals	Converts cellulose into sugar, as in the case of graminivorous feeders.—L.i./13,470.
Emulsin	Almonds.	Hydrolyses glucosides, <i>e.g.</i> , Amygdalin, <i>vide postea</i> , also Vol. I., p. 151.
Erepsin	Mucous membrane of small intestine.	Forms simple amino acids from proteoses and peptones.
Fibrin Ferment <i>see Thrombin</i>		
Inulase	Inula helenium and Squill.	Decomposes inulin, forming fructose.
Invertase or Sucrase	Intestinal juice and yeast.	Can convert many times its own weight of cane sugar into glucose and fructose.
Lactase	Animal body.	Converts lactose into glucose and galactose.
Lactic Acid Ferment (organised)	Lactic Acid bacteria <i>q.v.</i>	Converts lactose into Lactic Acid.
Lipase	Pancreatic juice and seeds of plants.	Converts fat into fatty acids and Glycerol.
Myrosin	Mustard seeds.	Hydrolyses the mustard glucoside in the presence of water.
Oxidases, see Catalase and Peroxidase		
Papain	The juice of <i>Carica Papaya</i> .	Digests proteins in acid or alk. sol. <i>Cf.</i> Vol. I., p. 651.
Pepsin	Stomach, <i>e.g.</i> , pigs.	Converts proteins into metaprotein, proteoses and peptone, in Acid solution only. <i>Cf.</i> , Vol. I., p. 661.
Peroxidase	Blood, milk and many plant tissues, <i>e.g.</i> potato and fungi.	Oxidizer. Sets free Oxygen from H_2O_2 . When an organic peroxide is in the plant tissue the system is called oxidase.
Perhydridase	Ditto.	Reducing agent.
Ptyalin	Saliva of the mouth.	Converts cooked starch into dextrin and maltose.
Rennin or Chymosin	Stomach of sucking animals, <i>e.g.</i> calf.	Coagulates the casein in milk, effecting clotting. <i>Cf.</i> , Vol. I., p. 661.
Steapsin, or Lipolytic Ferment	<i>see Lipase</i>	
Thrombin	Blood, after it is shed, in the presence of Ca. salts.	Coagulates fibrinogen into fibrin, forming the clot.
Trypsin	Pancreas.	Converts proteins into amino acids and a polypeptide in dilute alkali, Vol. I. p. 637.
Urease	The Soy Bean and in urine, especially in catarrh of bladder.	Converts urea into Ammonium Carbonate, <i>v.</i> Urine chapter.
Zymase	Yeast.	Converts sugars into alcohol and CO_2 , Vol. I., p. 279 <i>et seq.</i>

Coenzymes or Activators accelerate the action of enzymes, *e.g.*, *Enterokinase*, the constituent of the intestinal fluid which activates tryptase or trypsin.—L. i./13,470.

E. H. Farr, in his Pres. Add. B.P. Conf., 1914, gave an interesting account of enzymes of which he states 120 are known. He pointed out the methods of stabilisation that are used in France for herbs and at the same time indicated that our methods should not be hastily altered seeing that our drugs have gained repute on non-stabilised material.

In some cases several enzymes may take part in the hydrolysis of a glucoside. With the complex **emulsin**, for instance, the hydrolysis of amygdalin takes place in three stages:

1. Amygdalase resolves amygdalin into amygdalic nitrile glucoside and one molecule of glucose.

2. Beta-glucosidase hydrolyses the amygdalic nitrile glucoside into amygdalic nitrile and glucose.

3. *d*-Oxynitrilase decomposes the amygdalic nitrile into benzaldehyde and HCN.

Lipase. Action on Lecithin.

It has been suggested that Lipase might be employed to split up Lecithin in the treatment of malignant disease (*cf.* Vol. I., p. 763). We made a number of experiments on the matter. Castor Oil Lipase is however unsuitable. It cannot be purified from adherent Ricin, and we have proved would be dangerous to inject.

Saliva contains a lipase which is destroyed at 65° C. and has optimal pH = 7. It is activated 300 % by Calcium Chlorate and Sodium Oleate.—B.C.A., Sept. '28, 1047.

Vitamin 'A' Concentrates appear to accelerate lipase activity.—B.C.A. Nov. '28, 1282.

Rennin.—Differs widely from Pepsin. It is a decomposition product of protein, of Acid Albumin type, not precipitated by boiling the solution (*cf.* Pepsin). It dialyses through parchment but is hydrolised in the process (the main bulk in the case of Pepsin is not dialysed). Rennin is precipitated on saturating the liquid with Sodium Chloride. Proteolytic activity does not seem to be a part of the true physiological characteristics of Rennin.—Jl. Am. Chem. Soc. 1923, p. 249, per C.D. Mar. 31/23, 437.

ERGOTA.

In Vol. I. we deal fully with the active principle of Ergot to which reference is to be made.

Ergot was found to become 7 or 8 times weaker after being kept one year, whilst aqueous extracts of Ergot begin to lose activity in a few hours.

It has been suggested that Ergot might possibly be cultivated on nutrient media made from cereals such as wheat and rye.

The Annual Report of the Medical Research Council for 1922—1923 includes data on the investigation of Ergot.

Assay of Ergot Preparations.—In the U. S. P., X. Biological Test a dose not exceeding 0.5 Cc. per kilo of the fluid extract, injected intramuscularly to single-comb white Leghorn cocks, should produce a darkening of the comb corresponding to that caused by a standard extract prepared according to directions.

Ergot preparations are tested at the Pharmacological Laboratories of the Pharmaceutical Socy. of Gt. Britain on the lines of the U.S.P., where a composite fluid extract, made once a year from numerous samples of Ergot, is used as a standard.—J. H. Burn, P.J. ii./26,577; i./27,356. Query as to validity of this test.—E. W. Mann, *ibid* 633.

The usual standardisation by the **Cock's Comb Method** (causing gangrene), giving varied results due to the varying susceptibility and increased susceptibility with repeated injections, together with the non-dependability of other methods, led to the trial of a susceptibility procedure, based on the action of Ergot on the isolated rabbit's uterus. In this method the Ergot alkaloids paralyse the motor sympathetic endings in the uterus, and the action is unaffected by the presence of amines such as Histamine and Tyramine. With the isolated guinea-pig and the cat's uterus, *in situ*, results giving an indication of the amine content were obtained. The method of **Adrenalin reversion** can be used to measure the alkaloidal content, the results agreeing

well with those obtained by the cock's comb method. Liquid Extract of Ergot, *B.P.* was found to be almost completely devoid of Ergot alkaloids. Further plea for modification.—W. A. Broom and A. J. Clark, *Jl. Ph. and Exp. Ther.*, Vol. XXII./23,59. *P.J.* ii./23,89.

Until a better correlation exists between clinicians and chemists, to establish the identity of the constituent most useful in medicine, the Cock's Comb Test may be regarded as the most dependable.—H. A. D. Jowett, *P.J.* ii./23,511; see also H. C. Hamilton, *ibid.* i./24,131.

Not one ounce of the thousands of gallons of Ext. Ergot. Liq. made according to the *B.P.* '14 can have been of the slightest medicinal value. The clinician cannot form any opinion of the value of his remedies in many cases.—Second Report 1927, Pharmacol. Labs. Ph. Socy. of Gt. Britain, *P.J.* i./28,126.

Histamine (B-iminazol-ethylamine) in large doses produces symptoms very like those of anaphylactic shock and the latter has many features in common with surgical shock. Its vasodilator action seems to be on the capillaries rather than on the arteries or arterioles and the fall of pressure in surgical shock is almost certainly due to a similar capillary dilatation.—*Abst. Ann. Rep. Chem. Soc.* 1919 (Vol. XV.), p. 151.

Histamine is present in small amounts in enzymatic products, *e.g.*, Witte's Peptone; it is found among the hydrolytic products of crystallised albumin and casein, and may be obtained from acid-treated tissues, *e.g.*, the liver, the posterior lobe of the pituitary, and other tissues, such as the gastric mucosa, especially when precautions are taken to avoid bacterial contamination. It has been isolated from the intestinal wall of the ox and from aqueous extracts of the fish called *Maguro* (*Thymus thunnus*).

It is not considered that Histamine is present as such, or in the tissues of the living animal, but as a labile precursor, from which it is liberated by acid and heat employed in the treatment of the organ extracts. Protein metabolism of the body may be its true source. Injected subcutaneously into human beings, it produces a violent and intense erythema all over the body, headache, conjunctivitis, paræsthesias, vomiting, tenesmus, bronchial spasm and unconsciousness.—J. J. Abel, *Jl. Ph. Exp. Ther.*, Feb. '24/1.

Injury to, or irritation of, the skin causes liberation of Histamine or an allied body which produces the reddening.—per Pres., Oct. '28,317.

Histamine derivatives.—*B.C.A.* '28,A.1145.

The stimulating power of Histamine Phosphate on the ureter is greater than that of Pituitary Extract. It increases the general tonus of the ureter.—C. M. Gruber, *Jl. Pharm. and Exp. Therap.*, Oct. '28,207.

Further on Histamine, see Vol. I., pp. 406, 666, 670, 673, and Pituitary Gland, p. 966.

History and Chemistry of Ergot.—Outbreaks of Ergotism in the sixteenth century in Germany (Hessen). There was little in England, probably because rye was little cultivated here. Epidemics ceased about 1770. A complete statement of the chemical constituents.—G. Barger, *P.J.* ii./20,470.

Ergot poisoning among rye bread consumers amongst Jewish population of Manchester.—*B.M.J.* i./28,301.

FERRUM.

Pharmacology of Iron.

Ferrous compounds are not precipitated in the highest concentrations of protein solutions or in blood serum, nor do they agglutinate or dissolve washed erythrocytes. They have neither an irritating or astringent action on subcutaneous or intravenous injection.

Ferric salts are precipitated by dilute protein solution and they agglutinate and dissolve washed erythrocytes. The hæmolytic action of Ferric salts of organic or Hydroxycarboxylic acids is stronger than that of inorganic salts.—*B.C.A.* '27,A.172.

Inorganic Iron whether given by the mouth, intravenously, or subcutaneously is absorbed, and is found especially in the liver and spleen, but is not converted into hæmoglobin. The prescribing of Iron for anæmia following hæmorrhage is futile. The efficiency of **food iron** seems pronounced.—*Jl. A.M.A.* ii./25,1141.

Pilula Ferri (B.P. '14).

A little Reduced Iron added would prevent oxidation. The employment of sodium bicarbonate in place of sodium carbonate, together with plenty of water, a little honey and gum acacia, makes a pill which will keep unoxidised for a long time.

Iron acts more as a stimulant to the blood-forming organs than as a constituent of new blood. In whatever way it enters the blood corpuscle iron is an essential factor in treatment.

Patients suffering from chlorosis improve more rapidly under a ferrous carbonate preparation so far as hæmoglobin content is concerned, than under Iron-protein preparations.

THE FATE OF IRON GIVEN BY THE MOUTH.—In cases where large doses of Iron failed to increase hæmoglobin, 63 to 83% of Iron given by the mouth was found unchanged in the fæces, but among cases whose hæmoglobin was increased by large doses the discharge of unchanged Iron was up to 18% less. No difference in amount discharged whether patient had, or had not, free Hydrochloric Acid in gastric juice, and the amount of unchanged Iron found in fæces was the same whether large or small doses of reduced Iron were given. Authors conclude that the best therapeutic results are obtained with large doses.—B.M.J.E.i./24,42.

Ferrous Carbonate Estimation.—Remove the coatings from two pills and weigh. Dissolve in a small quantity of water, say, 15 Cc. with sulphuric acid 5 Cc. Titrate with N/10 potassium bichromate, using potassium ferricyanide. Multiply the number of Cc. of Bichromate solution used by 0.0115 to obtain the amount of ferrous carbonate in grammes in the two pills. *References on the matter in 17th edition, p. 72.*

DIPHENYLAMINE is better than Ferricyanide in titration.—F. J. Dyer and W. B. Forbes, B.P.C. '26; P.J. ii./26,167; C.D. ii./26,253.

Iron in Blood.—Determination of, as Sulphocyanide, by means of a colorimeter.—Y.B.P., 1922,35. (A colorimeter could be improvised.)

Iron Content of Foods.

Of 150 common food materials examined the figures for Iron content range from 0.00015% for lemon juice to 0.0192% for parsley. Arranged in descending order—dried legumes, green leafy vegetables, dried fruit, nuts, cereals, poultry, green legumes, roots and tubers, non-leafy vegetables, fish and fruits. Cabbages, celery and head lettuce are low in Iron: salt-water fish contain more Iron than fresh-water fish, and fish with dark-coloured tissue more than those with light-coloured, and the dark meat of poultry more than the light meat.—Jl. A.M.A. ii./28,251.

Ferri et Ammonii Citras Viridis.

To prepare a scale compound of ferric ammonium citrate of a *green* colour, as distinct from B.P. '14 which is dark red, the proportion of acid should be raised to one molecule and a half of citric acid to one atom of ferric iron. Larger quantities of citric acid heighten the green colour, but the salt becomes more hygroscopic.—R. C. Cowley, C.D. i./11,315.

Some experiments by us on this matter showed that the proportion of Ammonia is also of importance. Very light green scales can be produced by using only $1\frac{1}{2}$ molecules of Citric Acid to 1 atom of "ic" Iron and $1\frac{1}{2}$ molecules of NH_3 . This yields a preparation containing 22% Fe_2O_3 .

A minimum of 5.5% Ammonia is more than necessary to ensure stability in aqueous solution.—G. J. W. Ferrey, P.J. ii./28,87.

Syrupus Ferri Iodidi.

The addition of Hypophosphorous Acid in U.S. is objected to—it is the instability of Ferrous Iodide that makes it so valuable therapeutically. The absorption of the Iodine is required—added preservative prevents this. It is recommended to use more iron as follows. Place Iron Wire 25 Gm. in a 500 Cc. flask and wash well with water, add Water 150 Cc. and then Iodine 41.5 Gm. Shake, and when the mixture is of greenish colour and free from Iodine odour boil for five minutes. Filter through a folded filter paper, the point of which dips below the requisite 700 Gm. of Syrup. When the liquid has run through, wash the flask and filter with a mixture of Syrup and Water each 25 Cc., previously heated to boiling, finally make the weight 1,000 Gm.—P.J. ii./10,576.

Citric acid $\frac{1}{2}$ % is even stronger than hypophosphorous acid as preservatives.

Ferro-Silicon.—A physico-chemical alloy of Iron and Silicon used in the manufacture of steel goods where easy working and high tensile strength is required. In contact with water or moist air gives off poisonous gas, *i.e.*, Phosphoretted Hydrogen, Arseniuretted Hydrogen, *inter alia*, hence dangerous unless correctly used. That containing between 40 to 60% Silicon contains the most impurities.—L. ii./10,220.

Syrupus Ferri Phosphatis Compositus.

Estimation of Iron and Calcium.—The estimations of Iron and Calcium in this preparation have to be conducted separately.

Iron.—Dilute 20 Cc. of the Syrup with water considerably, heat on a water bath, add Ammonia in slight excess and allow precipitate to deposit on the water bath. Collect and wash quickly with boiling water. Ignite and dissolve in Hydrochloric Acid, add Ammonia in slight excess, collect and wash slightly and dissolve in dilute Sulphuric Acid. Reduce by boiling with copper foil and titrate with Permanganate. The iron is expressed as Ferrous Phosphate

Calcium.—Add about 1 to 2 Gm. of Citric Acid to 20 Cc. of Syrup and a little Hydrochloric Acid. Make slightly alkaline with Ammonia and finally just acid with Acetic Acid. Add Ammonium Oxalate in excess and estimate Calcium as usual.

FILIX MAS.

Extractum Filicis Liquidum (B.P. '14).

See also Vol. I., p. 422.

The Sp. Gr. of the liquid extract should not be below 1.0 (B.P. '14) R.I. at 20° C., not below 1.5, usually 1.505 to 1.509. Must dissolve entirely in 10 volumes Petroleum Ether. Saponification value 230 to 250. Unsaponifiable matter 8 to 11%. Fatty Acids should have mean combining weight of 240 to 255. Crude Filicin not less than 20% (B.P. '14 requirement). At one time it was systematically adulterated with castor oil.—E. J. Parry.

P. Helv. requires 26—28% Crude Filicin. This is higher than usually found.

GELSEMI RADIX (B.P. '14).

A standard of 0.5% total alkaloids for the root, and 0.05% for the tincture, has been suggested.

Older refs. on the Alkaloids are provided in Edn. XVII., Vol. II., p. 74, 75 and Y.B.P., 1920, p. 10.

Identification of Gelsemium.—It does not contain any Aesculin. The fluorescent body is Scopoletin (Aesculetin—5—Methyl Ether). If 0.5 Gm. of the ground drug be heated in a tube with Chloroform, the mixture filtered and the filtrate shaken with water to which a few drops of Dilute Ammonia have been added, the aqueous layer on separation shows distinct blue fluorescence, indicating presence of Scopoletin.—F. Tutin, P.J. i./12,157.

GLUCOSUM (B.P. '14).

Glucose may contain sulphur dioxide and hence be unsuited for pharmaceutical syrups, causing change in colour and production of odour.

Test—To 10 Gm. dissolved in water *q.s.* to 50 Cc. add 1 Gm. Sodium Hypophosphite and then Phosphoric Acid (1.5) 10 Cc. Cork the container and place in a warm place for a few hours. The sulphur compounds can then be detected by odour.—W. B. Cowie, P.J. i./16,235.

GLYCERINUM (B.P. '14).

Glyceryl Carbonates.—Glycerin and Phenyl Carbonate react at moderately high temperatures in vacuo. The completely saturated product is a solid crystalline substance with M.Pt. 138° C.—insoluble in water. Phosgene may also be used.—Patent 19,924 of 1911, *vide* P.J. ii./12,299.

Ultra violet rays from a powerful Mercury-quartz lamp decompose Glycerin with formation of Formaldehyde.—P.J. ii./12,7.

was quite bright, all the rest showed strong growth. Inoculation of MacConkey's broth showed that No. 3 was sterile, all the rest giving growth. No. 3 gave a distinct reaction for Formaldehyde by Rimini's test, No. 4 gave none. This proves that although the proportion of Formaldehyde is (to our knowledge) insufficient to kill *B. Coli*, nevertheless, the small amount slowly generated from the Hexamine is sufficient to inhibit growth of the organisms and thereby to have a marked influence on bacilluria.—W. H. M., 1914 Experiments.

Experiments and clinical work by others indicate similar conclusions. Cf. Vol. I., pp. 450, 451. Knott has shown that Hexamine is antiseptic in presence of alkalinity. McDonagh says that to view the activity of Hexamine as due to Formalin is a myth.

Sterilisation of Hexamine Solutions.—Having occasion recently to prepare sterile solutions of Hexamine for *Intravenous use* (cf. Vol. I., p. 457) both of 15 and 40% strength, the point arose as to whether the Hexamine would be decomposed by heating at 100° C. It was determined that prior to heating, the 15% and 40% solutions contained respectively 6 and 16 parts Formaldehyde per million, and after heating 20 minutes at 100° C. the content was 100 and 200 parts. In the case of 15% solution the amount of Formaldehyde is 1 in 10,000 or 1/60 grain in 10 cc. The quantity is negligible.

HYDRARGYRUM (B.P. '14).

Mercury, Detection of in Human Hair.

An amount corresponding to 1 in 90,000,000 can be found, using 2 to 10 Gm. of the hair, in those who have undergone Mercurial treatment.

Free the specimen from grease by washing with ether, alcohol, and water, then digest in hydrochloric acid containing potassium permanganate. On complete solution treat with H_2S . Collect pp. and treat with Potassium Chlorate and Hydrochloric Acid. Filter and evaporate to small bulk. Boil gently a strip of copper foil in same. Dry the foil and place in a tube one end of which ends in a capillary. Exhaust and seal, then heat in a flame so as to sublime the mercury in the capillary. Globules may then be seen under the microscope.

Hydrargyrum cum Creta (B.P. '14).

In the preparation of this, it is a good plan to add a few drops of Ether to the Mercury in the mortar—then fan to remove the bulk of it and finally add the Chalk with moderate trituration.—P. Boa, C.D. '20, 279. See also D. B. Dott, P.J. ii./20, 131.

Hydrargyri Subchloridum.

Finely Divided Calomel. (Duret.)

Dissolve Sodium Bicarbonate 6 Gm. and Glucose 10 Gm. in Distilled Water 80 Cc. Then dissolve separately Magnesium Chloride Cryst. 7.5 Gm. in water 20 Cc.

Mix the above and add to a third solution consisting of Mercuric Chloride 11.5 Gm., Hydrochloric Acid 10 drops and water 100 Cc. Shake well and allow to stand. Carbon Dioxide is evolved. When this slackens warm on water bath until no more gas comes off; wash and dry the precipitate. Yield 10 Gm. of a light form of Calomel which may be more active for local use.

Calomel made by this formula is similar to the scaly calomel recommended by Burden Cooper some years ago for ophthalmic use.

Prophylactic Ointment. (Duret.)

Calomel made as above 10, Magnesium Chloride Cryst. 10, Sodium Bicarbonate 7, Thymol 0.15, Camphor 0.35, Glycerole of Starch 15, Arachis Oil 15 Wool Fat 20, Water 25.

Triturate the Magnesium Chloride and Sodium Bicarbonate with the water, add the Calomel and the Glycerole of Starch, melt the Wool Fat with 10 Gm. of the Arachis Oil, and to this add the Thymol and Camphor dissolved in the remaining 5 Gm. of Oil. While still liquid add this to the first mixture and beat together until homogeneous. As a mercurial preparation it is well absorbed.—B.M.J. i./19, 713.

'Packets' for Venereal Disease.—The Ointment is Calomel 33, Lanolin 67, Vaseline 10. The other packet is Potassium Permanganate to produce 1 in 1,000 solution for washing.—P.J. i./20, 576.

Hydrargyri et Potassii Iodidum.

Mayer's Reagent. **Tanret's Reagent** is identical in composition.

Mercuric Chloride 13.546 grammes, Potassium Iodide 49.8 grammes, Distilled Water to 1 litre. This reagent gives a precipitate with alkaloids.

Formerly methods of volumetric estimation of alkaloids by means of the above were in vogue, but the composition of the precipitates is variable.

Mercury-Potassium Iodide Tablets for Lotions.

Syn. Biniodide Tablets.

We prepare these to contain $8\frac{1}{2}$ grains of Anhydrous Mercuric Potassium Iodide ($\text{HgI}_2\cdot\text{KI}$) with a sufficiency of Potassium Iodide in excess to make the body $\text{HgI}_2\cdot 2\text{KI}$ as explained Vol. I., p. 464. One dissolved in 1 pint of water makes a 1 in 1000 Solution of Mercuric Potassium Iodide.

These contain 6.4 grains of Mercuric Iodide HgI_2 (*cf.* P.J. ii./27,479,576). A trade custom has developed, however, of making them on various assumptions, *e.g.*, to contain $8\frac{1}{2}$ grains of the soluble Iodide $\text{HgI}_2\cdot 2\text{KI}$, which renders the content of Mercuric Iodide in the solution far less, namely, 5 grains.

There are various formulæ assigned to Mercuric Potassium Iodide—solid and in solution, and these form the basis of scientific disagreement and commercial advantage. So far as this work is concerned, the **Mercuric Potassium Iodide basis** as first mentioned is *intended*.

To estimate the Mercury in Lotion Tablets of this kind, Formalin reduction as recommended by E. Rupp is used. For the Iodine the Iodate Reaction in presence of strong Hydrochloric Acid. $2\text{HI} + \text{HIO}_3 + 3\text{HCl} = 3\text{ICl} + 3\text{H}_2\text{O}$. The whole matter is well dealt with in a paper by A. J. Jones, C.D. 20,523.

Hydrargyri Oxycyanidum.

Manufacture.—To obtain the pure salt, Mercuric Cyanide 40 Gm. and yellow Mercuric Oxide 30 Gm. are mixed and then made into a smooth cream with water 15. On stirring reaction occurs and almost a jelly is produced. 0.5 Cc. of Caustic Soda Solution 20% is then added with further stirring. The colour rapidly changes and the mass stiffens. Water is added to make the mixture workable and it is allowed to stand overnight. Dilute with water 200 Cc. and render acid to Phenolphthalein with Acetic Acid. Transfer to a flask containing about 700 Cc. of boiling water with 20 Gm. Mercuric Cyanide in solution. Continue heating until dissolved and set aside to crystallise.

The pure substance is dangerous. It explodes at 190°C . It begins to decompose at 160°C . The product of commerce is about 34% Oxycyanide and 66% Cyanide. See Vol. I., p. 460.

Unguentum Hydrargyri.

Several new formulæ suggested, *e.g.* Mercury 300, Hydrous Lanolin 15, pale yellow Beeswax $7\frac{1}{2}$, Benzoated Lard $47\frac{1}{2}$.—J. H. Franklin, P.J. ii./28,85.

Unguentum Hydrargyri Nitratis.

Martindale's Formula for Citrine Ointment.—Use only one-third of the B.P. '14 quantity of Acid and a volume of water equal to volume of Acid to dissolve the Mercury (in the cold), also employing White Vaseline in place of the lard, and a temperature of 87°C . for mixing. Stir until cool and smooth. Even this reduced quantity of acid is more than theory demands for making Mercurous Nitrate (and slightly more than theory for Mercuric Nitrate), but excess of acid appears to be necessary for keeping qualities. Furthermore, the water we found was also desirable. This ointment examined three months after making was of good colour, smooth, and easily rubbed into the skin.

(NOTE.—B.P. '14 maintains temperature 90°C . until frothing ceases)—the mixed lard and oil has initial temperature 150°C .

The principle on which the official ointment is made appears to be that the Nitric acid acting upon the mercury in the cold produces Mercurous Nitrate and Nitrous Acid, an excess of Nitric Acid being present. On adding to the fat the Nitrous Acid forms elaidin, and the heat of the fat causes oxidation of the mercurous salt with formation of more Nitrous Acid from the excess of Nitric Acid present. The excess of Nitrous Acid is driven off in the form of Oxides of Nitrogen.

The Mercury in the B.P. Ointment is, in the main, not in the form of Mercuric Nitrate, but on the contrary at least 50% of it is in the condition of salts of fatty acids or their oxidation products, and all the Nitric Acid is decomposed or dissipated by the process.

Mercurochrome.

(See also Vol. I., p. 479.)

The various specimens on the market differ markedly in chemical composition. Toxicity appears to bear a direct relationship to purity and the nearer the composition approximates to theoretical requirements the better the therapeutic efficiency and the lower the toxicity. A 1% solution frequently gives rise to Mercurial poisoning, but a 0.4% solution is relatively free from this objection.—John Eyre and Sir W. J. Pope, B.M.J. ii./28,239.

Estimation of Ionised Mercury in Mercurochrome.

The following is the method used in the author's laboratory :—

Take 50 Cc. of a 1 in 1500 solution and acidify with Hydrochloric Acid. Filter. The resultant solution should be clear and bright and practically colourless. Place in a 'Nessler' glass and in a similar 'Nessler' glass place 50 Cc. water. Add to each 1 Cc. 1.5% Sodium Sulphide solution. A darkening in colour indicates the presence of ionised Mercury. To estimate the amount match by adding to the 50 Cc. water a solution of HgCl_2 1 in 10,000. 1.65 Cc. of this solution = 0.37% ionised Mercury in the sample, and *pro rata*.

Three samples of commerce (6.7.29) showed a *practically identical amount*, viz. 0.7% approx. of ionised Mercury.

The following are recent additional Notes to those contained in Vol. I.

Intravenously in gonorrhœa and prostatitis 20 Cc. 1% solution followed by severe rigor, temperature of 105° F., and passing of crimson urine. Moral effect terrific but therapeutic effect doubtful.—L. i./28,209.

Extremely toxic to nervous system; intraspinal injections cause death rapidly.—per Pres., Jan. '28,7.

HYDRASTIS RHIZOMA.

Assay Method.—The drug in No. 60 powder is treated with ether, ammonia and water. A volume of the filtrate is shaken out with sulphuric acid and water. The acid solution is rendered alkaline with ammonia and shaken out with ether, the ethereal solution is evaporated and the residue weighed. U.S. X. process is on this principle (not less than 2.5% alkaloids). B.P. '14 is not standardised, though the Liquid Extract *infra* is.

Hydrastina (Alkaloid).

To distinguish from Hydrastinine :—A solution of about 0.1 Gm. in 10 Cc. dilute sulphuric acid shows no blue fluorescence, but on gradually adding Potassium Permanganate Solution 1 in 10, avoiding excess, the fluorescence develops. (U.S. IX.)

Hydrastinine Hydrochloride. *To detect Hydrastine.*—In an aqueous solution of the salt (1 in 20) Bromine water produces a yellow precipitate which is completely soluble in Liquor Ammonia, producing an almost colourless solution.—U.S.

For Foreign Alkaloids.—A few drops of Ammonia Solution added to 1 Cc. of a 1 in 20 aqueous solution produces no turbidity.—U.S. IX.

HYDROGENII PEROXIDI LIQUOR.

P.G. VI. gives method of estimating by titrating Iodine liberated from Potassium Iodide.

Preservatives.

BENZOIC ACID 0.05% added to Hydrogen Peroxide Solution is said to be a good preservative.

ACETANILIDE 0.002% with Hydrochloric Acid 0.02% or with Phosphoric Acid 0.1% will keep 10 vol. Hydrogen Peroxide for several weeks. The first combination was best of the series, but the loss in strength is nevertheless grave. The loss after keeping 4 years amounted to 70 to 99%.—H. R. Jensen. B.P. Conf. 1920.

ETHYL ALCOHOL added in proportion of 10% by volume has been suggested.

HYOSCINA.

For details as to isolation of the alkaloid in Toxicology (the alkaloid withstands putrefaction) and of the Crippen case, see Edn. XVIII., Vol. II., p. 83

We found the alkaloid remained unchanged in putrified meat for two months.

Datura.—Applicability of mydriatic test in decomposed viscera.—Analyst '26,344.

HYOSCYAMI FOLIA. (B.P.'14).

Cultivation.—The plant is difficult to grow. Proximity to the sea-shore—often its natural habitat—is an essential. The tops of the young biennial plants die down in the autumn, and the roots remain quiescent during the winter. Hence many of the plants succumb to the weather conditions and insect parasites. Self-sown plants—in waste places and on rubbish heaps—often attain a height of 5 feet or more. It grows wild on the north coast of Somerset.

Hyoscyamus Seed from wild plants germinated well and gave biennial crop, while commercial seed is not good.—T. W. Hazelby, P.J. i./21,227.

If the *whole* of the seeds of a biennial plant are saved and sown the seeds will consist of a mixture of different sizes, some being small and brown in colour. The latter are usually immature and will when dried float on water. These may be thrown away. If the seeds are sifted there will be a considerable proportion of smaller grey seeds. These produce the *annual* plants and the *larger* seeds will produce the biennial plants. Note chemical analysis of the plant solids—Phosphoric Acid 44, Magnesium 21, Potassium 18, Lime 6, Sodium 5. The excess of **Magnesium** over Calcium is rather unusual. It explains the liking for the **sea shore and Magnesian soils** (oolite, etc.) inland. Directions for culture.—E. M. Holmes, P.J. i./21,249.

The root is richest in total alkaloids and the annual plant is, if anything, a trifle richer than the biennial leaves either of the first or second year: thus Biennial Root 0.16%; Leaves biennial first year 0.059 to 0.069%; Leaves and tops second year 0.065 to 0.068%; Leaves and tops, annual, 0.064 to 0.07%.—S. Jensen, P.J. i./15,98.

The B.P. states the leaves of *H. Niger* collected from the flowering plants and dried are to be used in making the tincture. If the biennial leaves are used the tincture makes an opalescent or slightly milky solution with water. If the annual plant is used it makes a clear solution. The 'flowering tops' wording as in the 1898 B.P. might have remained.—E. M. Holmes, P.J. ii./15,6.

IODUM.

Historical.—Discovered by B. Courtois, 1811, in the mother liquor from alkali manufacture from sea weed. Discovery as an element (Humphry Davy). Distribution in Nature, Manufacture, Action and Therapy.—G. Sharp, P.J. ii./13,98. See also D. Curle, Pr. Dec., 1912,846.

Kelp Industry (see also Vol. I., p. 510).

Laminaria extraction for iodine is still practised to some extent in Scotland. The dried weed contains about 0.55%. Kelp-burning is also practised in France and Japan (and in Ireland.—W.H.M.). *Re Caliche* it is not possible to extract over 20% of the Iodine it contains. The International Combine, composed of the Chilean Association and the Scotch and French producers, arranges sales. World's output: Long tons in 1925, Chili 983, U.K. 25, France 53, Japan 16.—Imperial Inst. Brochure on Iodine, 1928.

Except where Guano or Chile Nitrate is used—we quote from a booklet by F. E. Corrie—**no iodine is restored to the soil**, which with every crop lifted, with every animal sent to the abattoir, grows consequently poorer and poorer in this vital element. Furthermore, many countries, *e.g.* Australia, New Zealand, Canada, Northern U.S.A., and the cattle country of Brazil, are naturally deficient in it. **The Argentine** campo was once rich in Iodine but in the last three or four decades it has been **literally eaten out of the soil**. Lack of Iodine has militated against the

live-stock industry. A little over $\frac{1}{2}$ grain of Iodine added as Potassium Iodide showed improvement in size and weight (10%) in pigs. Further, the Iodine-consuming pigs consumed less food and made more use of it.

We cannot agree, however, regarding the sweeping statement concerning the '50,000 cretins or imbecile dwarfs recognisable at sight in *Switzerland*—an Iodine-free country.' (In the course of a recent stay in that country—1928—we were amazed at the *wonderful physique* of the agricultural men and women, cutting broad swathes of grass with the scythe on the side of the mountain and carrying 4 or 5 crops a year up ladders into barns—feats which the English agricultural labourer would hardly attempt. Young cyclists, of splendid physique, clad only in short-sleeved vests and shorts, were on tour on the highways.—W.H.M.).

The next statement is that patchy wool is a concomitant of goitre in Canada and Iodine prevented it—'100%.' The matter was confirmed by the writer (F. E. Corrie) by experiments in Kent. *Orkney sheep with fine fleeces* are great eaters of *seaweed*. Iodine also improves milk secretion. Mineral mixtures are advised, *e.g.* for cattle and sheep:—Feeding bone-flour 40 lbs., fine ground limestone 40 lbs., Salt 20 lbs., Potassium Iodide 2 ounces.—Sept. '28.

In the Black Sea, about the middle of the triangle formed by Sebastopol, Odessa and in the mouth of the Danube, 30 to 50 metres below the surface, a spacious field of a red alga exists in which may be important quantities of Iodine; likewise in the Sea of Azof.—P.J. i./15,41.

Biochemical studies of Iodine.—B.C.A. '28, A.1152.

Red and Chinook Salmon contain 4 times as much Iodine as Butter and undergoes no apparent loss on canning. Canned Salmon should be included in the diet of goitrous patients.—Jl. A.M.A. i./26,1339.

Iodine in Natural Waters, see p.422.

ESTIMATION OF ORGANIC IODINE COMPOUNDS. It is a good plan to saponify with KOH 2 Gm., Water 12 Cc. and Alcohol 30 Cc. After cooling place in separator and make acid with H_2SO_4 ; add Chloroform and then a few drops of $NaNO_2$ Solution. Shake and withdraw the Chloroform, and then add a little more $NaNO_2$ and more Chloroform, and so on until all Iodine is removed. Wash with water, add $NaHCO_3$ and titrate with N/10 $Na_2S_2O_3$.—P.J. ii./11, 711, *cf.*, Thyroid Gland, Martindale's estimation process.

LIMIT OF COLOR PRODUCED BY IODINE VISIBLE IN CARBON DISULPHIDE, AND IN CHLOROFORM AND ETHER: In Carbon Disulphide and Chloroform we found decided mauve color is visible in 1 in 500,000 solution. In Ether the brown color is visible in the same dilution.

ESTIMATION OF THE 'IODINE NUMBER' OF A FAT OR OIL.

In the following methods, Chlor-Iodine addition products are formed of the glycerides of the unsaturated fatty acids and of the acids themselves that are contained in the oils so treated.

The Iodine number indicates the percentage of Iodine capable of absorption, and can be determined by the original method of Von Hübl, or by the more reliable and convenient modification proposed by Wijs.

Hübl's Method. The Iodine solution is prepared by dissolving Iodine 25 Gm. in 500 Cc. of Absolute Alcohol, and also Mercuric Chloride 30 Gm. in a further 500 Cc. of Absolute Alcohol, filtering and then mixing. After standing 12 hours or so, the strength is ascertained by standard Sodium Thiosulphate solution in the customary manner.

0.8 Gm. of the fat, or 0.4 Gm. of a non-drying oil, or 0.2 Gm. of a drying oil, is accurately weighed out by means of a weighing bottle or Sprengel tube, and dissolved in 10 Cc. of Chloroform or Carbon Tetrachloride in a 600 Cc. stoppered bottle. The Iodine solution, 25 Cc., is run in from a pipette, and if the mixture becomes decolorised on standing a short time a further 25 Cc. is added. After about 4 to 6 hours standing in the dark, 15 to 20 Cc. of 10% Potassium Iodide solution is added and the liquid diluted with about 400 Cc. of water. If there is any precipitate of Mercuric Iodide, more Potassium Iodide must be added. The free Iodine is determined with N/10 Thiosulphate and Starch, shaking thoroughly. A blank experiment, without

the oil, is conducted, and, from the difference in the two volumes of Thio-sulphate required, the amount of Iodine absorbed can be calculated, and this is then expressed as units per cent. of the oil.

Example.—0.8 Gm. of a fat required 48—19 Cc. of Thiosulphate Solution = 29 Cc. = 0.3651 Gm. Iodine, therefore 100 of the fat combines with 0.3651×100 Iodine = 45.6, which is therefore the Iodine

0.8

Number of the fat.

Wijs' Method.

The Iodine Monochloride solution is prepared by dissolving 13 Gm. of Iodine in about 800 Cc. of pure Glacial Acetic Acid, and then passing in Chlorine until the titre against Thiosulphate is doubled. When this point is reached, there is a sharp change in color from the brown to a brownish-yellow, and the solution is then made up to 1 litre with Acetic Acid. The Iodine value is determined as previously described, but, since the Wijs' solution has the advantage of keeping its strength unchanged for a considerable time, it is not necessary to conduct a blank experiment for each estimation, and, the absorption being more rapid, thirty minutes standing in the dark is usually sufficient, except for the drying oils which need 2—6 hours. For dissolving the fat, Carbon Tetrachloride is preferable to Chloroform.

Iodine Numbers of certain Oils and Fats.

Almond Oil 93—101.9.	Maize Oil 111—122.9.
Apricot-kernel Oil 100—108	Neatsfoot Oil 62—72.
Arachis Oil 85.6—105.	Olein (pure) 81.7.
Cacao-butter 34.0—37.7.	Olive Oil 77.28—88.
Castor Oil 83.4—85.9	Poppy Seed Oil 132.6—143.3. We
Coco Nut Oil 9.5 (but see also Vol. I., p. 102).	found recently 138.1.
Cod-liver Oil 155—173.	Sesame Oil 102.7—112.
Cottonseed Oil 102—116.9	Rape Seed Oil 97—106.
Human Fat 61.5.—L. ii./07, 691.	Soya Oil 121.3—123.2. (<i>Vide</i> also Vol. I., p. 860. We found only 80.8, with a doubtful sample).
Japan Wax 4.2—6.6.	Sperm Oil 81.3—85.
Lard 46—63.8.	Sunflower Seed Oil 119.7—135. We
Linseed (boiled) Oil 73.7—101.3.	found recently 136.1.
Linseed (raw) Oil 170—187.7	

McIlheney's Bromine Method is better than the iodine ones.—P.J. ii./09, 146, 201.

Halogen Compounds of fats formed by Hübl's Reagent.—P.J. ii./11, 437.

HYDROGENATED FATS.—Determination of Iso-oleic Acid content permits recognition. This has Iodine value of 90 and produces a Lead salt insoluble in organic solvents.—P.J. i./24, 537.

Thiocyanogen Value—a new constant of oils and fats—is of special use in determining the amount of Linolic Acid in an oil. Thiocyanogen, like Iodine, is quantitatively absorbed by substances containing a double bond, but with fatty acids containing a triple bond (Stearolic, Behenolic) there is no absorption; and with Linolic Acid there is only absorption of half the Thiocyanogen, corresponding to its Iodine Value.—Analyst, '26, 157, 264.

Commercial Resublimed Iodine in France has been found to contain traces of Sulphur. Probably due to use of Sulphite in making to reduce Iodates, any Calcium Thiosulphate formed would be precipitated with the Iodine and would yield some Sulphur on sublimation.—P.J. ii./25, 10.

"Propyl."

Iodine 1.25% in 70% *Isopropyl Alcohol* recommended as a substitute for the commonly-used Iodine in Rectified Spirit. An efficient antiseptic. Is not harmful to the skin, has penetration power and evaporation rate equal to Ethyl Alcohol, and costs much less.

It should be recently prepared.—J. Wicliffe Peck, L. ii./28, 444.

Iodinol 40% (*Martindale*).

Chemistry. An additive compound of Iodine and Poppyseed Oil containing 40% by weight of Iodine in combination. It is of pale yellow colour, Sp. Gr. 1.328; it can be heated to 100° C. without decomposition.

Uses.—With due care, it may be employed to render the bronchi and their ramifications opaque to X-rays, its chief value lying in its ability to show the presence or absence of non-obstructive bronchiectasis and when present, even

in the early stages, its locality, extent, and type. It is non-irritant to the mucous membrane, etc. After injection in the bronchi, it is absorbed in the lung and Iodine can be detected in the urine for many days after; hence it is an antiseptic agent rational in treatment in chronic affections of the lower respiratory tract. (For **Iodinol 25 % per os**, see Vol. I., p. 519).

Contraindications.—High fever or marked intolerance to Iodine, and in grave septic conditions of the lung, or active tuberculosis.

Method.—Test first for Iodine intolerance with Potassium Iodide 10 grains three times in the course of a day.

The amount used varies from 5 to 40 Cc., the average being 20 Cc. For outlining the bronchial tree, 6 to 10 Cc. is sufficient. (To lessen the viscosity the oil is first warmed in water at 100° F.)

Oral use.—Given the confidence and co-operation of the patient, this is best, but it is unsuited in children and nervous patients. The patient should be seated with his head on his hand and his elbow on a rest, the operator in front. The tongue is protruded and a blunt-ended cannula placed over its base, between the pillar of the fauces and the uvula. The warm oil (100° F.) is given with a 20 Cc. syringe, while the patient breathes slowly and regularly. If patient heaves, useless to continue. He should lean to the side injected, and then be semi-recumbent with head lowered.

The Crico-thyroid Membrane route.—The patient reclines on a couch with head projecting over the end, to keep the membrane stretched. To inject the bases of the lungs, the shoulders must be kept raised, and for the apices the patient lies flat during the injection, the head and shoulders being lowered after. A drop of Novocain solution to produce a small bleb is injected over the mid-point of the membrane exactly in mid-line. With a strong needle, 0.5 Cc. of 5% solution of Cocaine HCl. (warmed to 100° F.) is slowly injected through the spot into the trachea, and the patient can then sit up for 2 minutes and is allowed to cough. A 20 Cc. syringe filled with the Iodinol is attached to a trochar and cannula which has been inserted into the trachea. To be sure the needle is in correct position, withdraw the piston; bubbles of air should freely enter the syringe. With the patient in the right position he should breathe deeply through the mouth, avoiding swallowing and coughing, the injection being given slowly. Radiograph quickly, vertically and horizontally, afterwards placing a Collodion dressing on the spot. For the young or extremely nervous a general anæsthetic (Ethyl Chloride, open method) is given. After every injection screen the stomach to ascertain whether much of the oil has been swallowed.

Other methods are direct injection into the lung, the Bronchoscopic, the Transglottic, the Intubation, the Catheter, and the 'Swallowing' method.

Caution.—There is an element of danger in the above technique, *though with the oral method it is almost negligible*. The procedure is a serious one and should not be employed indiscriminately. The possible dangers are symptoms of Iodine poisoning (this only applies with the Crico-Thyroid route), injury to local tissues in the neck, and broncho-pneumonia resulting from dissemination of infection throughout the lung. Minor symptoms, which normally disappear in 24 hours, are injection malaise, anorexia, and headache. In pulmonary tuberculosis the injections are undesirable, and its use is dangerous in patients with advanced bronchiectasis with foul secretion.

The resulting pictures are excellent and there is no irritation of the mucous membrane.—F. G. Chandler, B.M.J. ii./28, 1157.

X-RAY PICTURES OF THE MALE URETHRA.—Shadows obtained with Iodinol 40% very satisfactory. No irritation of the urethral mucous membrane. A urethral pouch demonstrated at the Midland Medical Society.—G. P. B. Huddy, 6/6/29.

For giving shadows of the uterus and fallopian tubes found satisfactory at Cardiff Royal Infy.: No toxic symptoms.—W. Panes, 20/6/29.

Lipiodol—The use of opaque substances as an aid to the diagnosis in gynecological conditions.—R. A. Gibbons, B.J.R., Feb., '28, 37.

Pelvic suppuration following intra-uterine injection of Iodised oil in a healthy woman; should be confined to the diagnosis of sterility and the patient then told of the possible danger.—Sicard and Solal, per J.I.A.M.A. i./29, 847.

Sodium Bicarbonate before pleural examination produces gas in the stomach and renders bases of the lungs more visible.—L. S. T. Burrell and S. Melville, L. ii./29, 689.

IPPECACUANHA.

(See also Vol. I., p. 523.)

Historical.—The Brazilian root was first brought to Europe in 1648 by Pison. It was subsequently given for dysentery, chiefly in small doses, by several Anglo-Indian physicians. In 1858 E. S. Docker, I.M.S., introduced large doses (60 grains two or three times daily) for severe dysentery in Mauritius. G. Foy pointed out that we are indebted to Dr. J. L. Bardsley, of Manchester (1829) for the empirical use of Emetine in dysentery.

Paul and Cowinley stated the average composition of Rio and Carthagena alkaloids to be: Emetine in Rio 72 per cent., in Carthagena 40.5%; Cephaeline in Rio 25.9, Carthagena 56.8%. See also H. R. Jensen, P.J. i./16,519.

Extractum Ipecacuanhæ Liquidum (B.P. '14).

Alternative Estimation Process.—

Evaporate 10 Cc. of Liquid Extract in a flat basin with 5 Cc. of N/1 Acetic Acid and 10 Cc. of Water to 5 Cc. Twenty Cc. of water are added with 5 Cc. Acetic Acid and the resinous matter broken up and removed by filtering through a pledget of cotton wool into a cylinder. The capsule is washed with 10 Cc. water and 1 Cc. Acetic Acid. To the cold mixture is added 1 Cc. liquor ferri dialysatus (1885), the whole made up to 50 Cc., well shaken and set aside to separate.

Twenty-five Cc. are filtered off into a separator, mixed with excess of Ammonia and 20 Cc. of equal volumes of ether and chloroform, well agitated, warmed and set aside to settle. This extraction is repeated with another 20 Cc. of ether and chloroform mixture. Other two extractions are made with 10 Cc. of chloroform, which gives a more complete extraction. The bulked liquids are distilled off and the residue dried at 80° C. until weight is constant.

The weighed residue is dissolved in excess of N/10 HCl and back-titrated with N/20 NaOH, using tincture of cochineal as indicator.—W. B. Cowie, P.J. i./13,433. 1 Cc. N/10 HCl = 0.02867 Gm. combined or mean of emetine and cephaeline.

Tschirch found the P. Hung. assay method best:—Shake 5 Gm. of powdered root in a well corked Erlenmeyer flask with Ether 75 Gm. for 15 minutes. Add 4 Cc. of 10% Ammonia Solution and shake well for 15 minutes further. Set aside 15 minutes, then filter off 60 Gm. (= 4 Gm. of root) into a 200 Cc. stoppered flask. Distil off the solvent to dryness. The residue is twice treated with 5 Cc. of Ether and the Ether evaporated each time. On cooling, 30 Cc. of ether saturated with water and 10 Cc. of N/10 solution of hydrochloric acid are added. After solution has been effected, add 90 Cc. of water and a few drops of solution of iodeosin. Shake and set aside for five minutes, agitating gently from time to time. Titrate with N/10 solution of sodium hydroxide until the aqueous layer assumes a faint rose tint. The difference between the amount of Cc. of N/10 solution of hydrochloric acid and N/10 solution of sodium hydroxide solution multiplied by 0.0241 indicates the amount of alkaloids present in 4 grams of powder.—C.D. '20, 1371.

Vinum Ipecacuanhæ (B.P. '14).

The amount of true alkaloids (volumetric) used in compounding this preparation might fall as low as 0.07%, though the amount put into it must be 0.095 to 0.105% (gravimetric). The B.P. uses sherry, and the tannin content will cause precipitation of the alkaloids. The B.P. makes no suggestion as to alkaloidal strength, and the assay method used for the liquid extract cannot be properly applied in the case of the wines. Titration of the alkaloids in the assay of the liquid extract is better than gravimetric method.—H. R. Jensen, P.J. i./16,518.

Adsorbed Emetine made by means of **Aluminium Silicate** found effective in stopping the excretion of cysts and free from the gastric irritation common with Emetine Bismuth Iodide. A similar Cephaeline compound was found to be irritant. Similar compounds of Opium alkaloids with Hyoscyamine, Quinine, Acriflavine, etc., had been made.—H. R. Jensen, B.P. Conf., 1920.

Emetine Poisoning.—A case in the Courts in S. Africa at the end of 1928 turned upon the possible **cumulative effect** of Emetine. A child had had both injections and 'E.B.I.' *per os*. The prolonged administration of relatively small doses is more to be feared than what may be termed

heroic doses over the first few days of treatment. Serious indications of poisoning may occur from oral, intramuscular, or intravenous use. The curative dose for *schistosomiasis* would seem to be about double that needed in amœbic dysentery. Watch for abnormal pulse. 'Kidney Albumin' is a dangerous sign. Use cardiac stimulants.—F. G. Cawston, Jl. Trop. Med., Jan. 15, '29.

JABORANDI FOLIA.

P. Microphyllus is largely used in making pilocarpine and was official in U.S. IX. if yielding not less than 0.6% alkaloids.

FR. CX. directs *P. Jaborandi* to be used, but states that *P. Pennatifolius* is much employed. It states further that *P. Microphyllus* Stapf. (Maranham Jaborandi) is esteemed by manufacturers on account of its high alkaloid content, but is the most adulterated.

P. Pennatifolius, *P. Selleanus*, and *P. Trachylophus* are substitutes and differ from the leaf as described in B.P. '98.

P. Trachylophus contained as much as 0.75%.—Southall.

P. Racemosus.—Jowett and Pyman obtained Pilocarpine Nitrate=0.12 per cent. of the leaves but no other crystalline constituent (contrary to previous workers).—Proc. Chem. Soc., 1912, 28, 268.

Venezuelan Jaborandi, referred to as *P. heterophyllus*, yielded 0.25% total alkaloids and 0.04% Pilocarpine Nitrate.—Y.B.P. '23, 326.

Pilocarpinæ Nitræ.

For an aqueous solution of 2 Gm. in 100 Cc. $\sigma_D = + 82.2$ @18° Cc.—FR. CX. Pure Pilocarpine Nitrate melts at 177–178° C. Isopilocarpine Nitrate (the salt of an isomeride and conversion product of Pilocarpine) melts at 159° C. That in U.S. melts at 170 to 173°C. FR. CX. 177°C.

Detection of Pilocarpine and Quinine in Toilet Preparations. —The relative solubility of Quinine Chromate and insolubility of Pilocarpine Chromate is used.—P.J. ii./12, 317.

LECITHIN.

Lecithin is a Mono-amino Phosphatide. Phosphatides are complex bodies of more or less fatty nature which can be extracted from tissues by Alcohol, Ether, etc., and which contain fatty acids, Nitrogen and Phosphorus. They are of unstable composition.

On hydrolysis Lecithin yields Stearic Acid, Glycerophosphoric Acid and Choline.

Lecithins may be derivatives of either Stearic, Palmitic, or Oleic Acid, alone or mixed. Ovo-lecithin is generally assumed to be mainly Stearyl, i.e., Choline-distearo-glycerophosphate, and plant Lecithin to be mainly an Oleic Acid body, but the fatty Acids are not determined with certainty.

Lecithin Content of Various Substances in percentages—

Brain	16.0	Egg Yolk	12.0
Heart	4.5	Peas	1.2
Liver	4.3	Lupin Seeds	2.0
Kidneys	8.5	Ergot	1.7
Lung	1.5	Yeast (dry)	2.0
Spinal Cord	11.0	Barley	0.7
Nerve Tissue (dry)	17.0	Wheat and Rye	0.6
Blood Corpuseles.. ..	0.46	Green Peas	0.15
Mushrooms	0.9	Milk, see Milk Analysis.	

Examination of Lecithin.—

From our experience we recommend the following as tests for purity:—

(1) 1 Gm. should be soluble in 10 Cc. of Alcohol 90%, leaving only a negligible residue not exceeding 2.5%. 1 Gm. dissolved in 10 Cc. of Alcohol should not require more than 0.5 Cc. of N/1 Sodium Hydrate to neutralise (Phenolphthalein).

(2) All the Nitrogen should be present in the form of Choline, i.e., it should be Alcohol soluble.

(3) The total Phosphorus should be estimated. Lecithin should be entirely soluble in Chloroform indicating absence of added mineral Phosphates.

If the **Cadmium compound of 'Lecithin'** (the Cadmium Chloride method is the usual method of purification) is recrystallised from a mixture of Ethyl Acetate and 80% Alcohol the true lecithin can be freed from **Kephalin** and then liberated from its Cadmium compound by means of Ammonium Carbonate.

(4) The ratio of Phosphorus to Nitrogen should be approximately 2 : 1

Phosphorus should be 3.5—3.7%.

Nitrogen should be 1.9—2.0%.

Iodine Value should be 60—65%.

Lecithin, Determination of in Preparations.—Extract 1 to 2 Gm. of a Lecithin preparation, or 5 to 20 Gm. of a food stated to contain it, with 96% Alcohol—first in the cold and then twice under a reflux condenser. Then extract the insoluble portion with boiling Chloroform 2 hours. The combined Alcohol and Chloroform extractives are evaporated and the residues are digested two hours with 100 Cc. Chloroform to separate the Lecithin from Phosphoric Acid, Glycerophosphoric Acid, etc. To estimate Phosphorus Pentoxide in the purified extractive incinerate and oxidise with Sulphuric and Nitric Acids or ignite with Magnesium Oxide and bring to weight as Pyrophosphate in the usual manner. The factor 11.36 is used to convert the amount found of P_2O_5 into Lecithin.

Lipoids are an essential in the food of animals. Among the lipoids there is a series of definite phosphatides, of which the molecule consists of Glycerophosphoric Acid and a fat acid with a nitrogenous base.

Each organ of the body elaborates one or more specific lipoids.

These lipoids represent to the organs what the alkaloids represent to the plants. Lipoids from the organs of man are in no wise different from those of a dog, horse, etc., or even fish. Organs or glands which are insufficient or impaired are found to lack lipoids, their power to elaborate them from the materials of the blood being diminished.

For every organic affection it is said there is a lipoid which is its natural specific.

LITMUS, CUDBEAR, ORCHIL and TURNSOLE.

Litmus. *Syn.*, **Lackmus** (German), is a blue pigment obtained from *Rocella tinctoria* (*Discomyces*). Employed chiefly as an indicator for respectively acid and alkali as Litmus Paper, also in form of solution in Volumetric analysis. Litmus is made in Holland by fermenting lichens in presence of ammoniacal liquids and potash.

LITMUS SOLUTION (B.P. Appendix, 1914).—Boil litmus 2, with alcohol 90% 8 for 1 hour, pour off clear liquid, repeat with 6 and again with 6 parts of alcohol. Digest the litmus thus washed in distilled water 20, and filter.

In titration, all CO_2 must be removed by boiling before taking end reaction. Not suitable for weak bases. **Quinine, Morphine and Strychnine are neutral to it** and the acids in their salts can be titrated as if base were absent.

Carbon Dioxide only turns Litmus "wine red" when alkaline bicarbonates are present as impurities, otherwise it turns red just like any other acid.

LACMOID, also known as **Resorcin Blue**, is chiefly Diazo-Resorcin. Solution 0.2% in Dilute Alcohol employed as indicator closely resembles Litmus in reactions.

Cudbear. *Syn.* **Red Indigo.**

A purplish red powder obtained by the ammoniacal fermentation of *Lecanora tartarea* and other lichens, designated in Germany *Persio*, in France *Orseille de terre*. Excepting for the fact that it is in the condition of a fine powder it is virtually the same as **Orchil**.

Tinctura Persionis.—Percolate Cudbear 2½ ounces with 1 pint of a mixture of 90% alcohol 1, and water 2. Used as a coloring agent. Acids increase the red and alkalis change to purple.

The following process renders percolation more rapid :—

Filter paper or brown paper is torn up into shreds, soaked in water for some hours and the water poured off, when fresh water is added and boiled

to reduce the paper to a pulp, using an egg whisk. This is drained off while still hot and worked up with eudbear in a mortar and then placed in a percolator. Suggested formula: incorporate Eudbear, $2\frac{1}{2}$ ounces, with the moist paper ($1\frac{1}{4}$ ounces), percolate with stronger Chloroform water to produce 15 ounces and add Alcohol 5 ounces.—E. Quant, P.J. i./22,281.

Archil *Syn.* Orchil.

The word Archil, or more properly Orchil, was originally the name of the plant from which the dye which goes under the name is obtained. It appears that before the introduction of Archil into this country a similar dye obtained from certain lichens in Scotland was in use under the name "Cork." This is given in Miller's "Plant Names" as the name of the lichens yielding Archil.

It is made from various lichens, *e.g.*, *Roccella*, *Lecanora*, etc. The lichens are ground up and fermented with addition of stale urine or ammonia. Its production is similar to that used for Litmus except that the Potash is omitted. In commerce it is usually in the form of a pasty mass known as Archil (French, *Orseille en pate*).

Turnsole (Fr. *Tournesol*).

The familiar coloring used on Dutch cheeses. The word has been more particularly applied to a product from *Crotophora tinctora*, A. Juss (*Croton Tinctorium* Linné)—a native of Southern Europe and the Orient. Rags soaked in the juice of this plant are exported to Holland. They change color on exposure to Ammonia vapour, and this purple color can be extracted with water for the purpose in question. Turnsole was at one time supposed to form the coloring matter of litmus.

PERFUMES OF LICHENS.—In addition to their inherent perfumes lichens have considerable utility as basis of Pot Pourris.

MAGNESIUM.

Magnesium metal may prove dangerous in certain conditions, *e.g.*, when powdered and mixed with an equal quantity of Silver Nitrate and a drop of water added. Slight explosion with flash may occur. With Mercuric Nitrate there is vigorous reaction, brown fumes rise but no flash.

Magnesium and Palladium Chloride together in certain proportions will cause water to decompose at ordinary temperature.

Magnesia Mixture for estimation of Phosphates.

Solution of Magnesium Ammonio-Sulphate. Dissolve Magnesium Sulphate 20, Ammonium Chloride 40, in Water 160, add Ammonia Solution 84. Allow to deposit in stoppered bottle before use. Employed for the gravimetric estimation of phosphates. Ammonium Magnesium Phosphate is precipitated and converted by incinerating into Magnesium Pyrophosphate $Mg_2P_2O_7$, =222.694.

MALTUM.

Extractum Malti. *Assay.*

Malt Extract should convert its weight of arrowroot in 20 minutes.

(a) Mix Bermuda Arrowroot 1 Gm. with Water 100 Cc., boil 10 minutes, and when cold make up to 100 Cc.

(b) Dissolve Malt Extract 5 Gm. in water *q.s.* to produce 100 Cc.

(c) Tincture of Iodine 1 Cc. with Water *q.s.* to 50 Cc.

Warm 50 Cc. of (a) in a flask on the water bath to 100° F. Add 10 Cc. of (b) also at 100° F., mix and keep at this temperature for 20 minutes. Remove 4 Cc. of the solution and add 1 Cc. of (c). There should be no evidence of unconverted starch.

Estimation of Diastasic Power.

The resulting Dextrose may be titrated with Fehling's Solution, 1 Cc. of this = 0.005 Gm. Dextrose = 0.0045 Gm. of Starch converted thereinto.

A properly prepared Malt Extract contains 50 to 75% Maltose. Glucose and Dextrin are sometimes added as sophistications, and the Protein content is consequently lowered—the latter should be about 6% of the whole, or 8% of the total solids.

The **Diastasic Power** can be expressed as the percentage of Starch digested by a sample of Malt Extract in half an hour at 40° C., *i.e.*, a Diastasic Power of 500 means an extract digesting five times its weight of starch.

The late E. F. Harrison assayed Malt Extract by determining the amount of Maltose produced from a given weight using Anhydrous Potato Starch 1 Gm. in Water 100 Cc. with 0.2 Gm. Malt Extract. After half an hour at 40° C. the Maltose formed is titrated. If the Diastasic Power is over 500 repeat the test using less Malt Extract. Glycerin is a frequent addition and might be approved of for an Official preparation to extent of 5% by volume. Proteins might be 5% at least. A lower figure for Protein would point to added Glucose or other non-nitrogenous matter.

Diastasic power of Malt determined and expressed as Gm. of Maltose produced per 100 Gm. of Malt. Modification of Baker and Hulton's Process.—Y.B.P. '22, 104.

Adulterants.—Starch, syrup and molasses-syrup (from beet sugar) have also been used.

Incompatibilities with Malt Diastase.

We conducted experiments a few years ago on lines somewhat analogous with those carried out in the case of Pepsin and Pancreatic Ferments (*q.v.*; this Vol.) The chemicals and preparation were mixed with 600 Cc. of an Arrowroot Mucilage 1% strength, 30 Cc. of a 20% malt extract were added and the mixtures kept at 100° F. and examined at 15 and 30 minutes for unconverted starch.

Acids.—Various Inorganic and Organic, and Acid preparations, *e.g.*, Ferri Perchloridum and Pepsin preparations were found to be **incompatible** with Malt Diastase.

Per contra a large number of substances which might have been expected to have inhibitory action on the ferment are *compatible* and may be prescribed simultaneously when required. The subject is more fully dealt with in the 17th Edn., Vol. II., pp. 91–93.

Free **Ammonia** is stated to inactivate Malt Diastase.

MEL DEPURATUM (B.P. '14).

The honey of commerce melted on a water bath and strained hot, adjusted to Sp. Gr. 1.36 if necessary.

For neutralisation 10 Gm. of Honey after diluting with 5 volumes of water shall require at most 0.5 Cc. N/1KOH using Phenolphthalein as indicator—(Test for *rancid honey*).

Honey on incineration should yield not less than 0.1 or more than 0.8% residue (*Invert Sugar and Starch*).

U.S. X. gives the following:—

If 1 Gm. of Honey be triturated with 20 Cc. of ether in a mortar and filtered and the filtrate be allowed to evaporate and 1 drop of a 1% resorcin solution in Hydrochloric Acid be added, a pink colour may form which disappears in half a minute, but an orange, cherry or brown-red colour must not be produced. (*Artificial honey or added invert sugar*).

Biochemistry of Honey. Contains carbohydrate in a form ready for direct absorption.—L. ii./24, 1346.

Morphine see Opium.

Recent Drug Addiction Matters are under Cocaine.

NITROGLYCERINUM.

Assay of Nitroglycerin in Solutions and Tablets.

Pure fused Potassium Nitrate 0.722 Gm. is dissolved in Distilled Water, *q.s.*, to 1,000 Cc. and used as standard. One Cc. of this solution contains 0.0001 Gm. Nitrogen in form of Nitrate—thus 1.2 Cc. will contain the same amount of Nitrogen as $\frac{1}{10}$ grain of pure Nitroglycerin. If an Alcoholic Solution be the subject of analysis the equivalent of 0.00065 Gm. ($\frac{1}{10}$ grain) of pure Nitroglycerin (calculated) is measured out and allowed to evaporate spontaneously

In a dish and in another dish 1·2 Cc. of the standard is measured and evaporated at a low heat. When both are dry 2 Cc. of Phenol-disulphonic Acid Reagent are added to each—both are well stirred and left 10 minutes, diluted with water, rendered slightly alkaline with KOH and diluted to 100 Cc. or less in Nessler tubes and compared. For Tablets, 5 tablets are powdered, dissolved in 10 Cc., filtered and 2 Cc. of the filtrate (or equivalent of $\frac{1}{10}$ grain) treated as above.

Phenol Di-Sulphonic Acid Reagent.—Heat Phenol 3 Gm. with Sulphuric Acid 37 Gm. in a flask on a water bath at or near 100° C. for 6 hours—Sutton's Volumetric Analysis.

We have found the method to give concordant results with Alcoholic Solutions of Nitroglycerin, but it is not suitable for the Tabellæ as made by the writer.

Nitroglycerin is rapidly decomposed in the body and is unlikely to be found in the liver or in the urine. It might be extracted with Ether from stomach contents.—P.J. 1/26,406.

NUTRIMENTA.

For the maintenance of health and for satisfactory growth the food intake, in addition to Oxygen and Water, must consist of the following factors :—

- (1) PROTEIN either from plants or animals.
- (2) FATS.
- (3) CARBOHYDRATES, or Starches, Sugars, and Cellulose.
- (4) Certain INORGANIC SALTS.
- (5) At least five VITAMINS, A, B, C, D and E.

Proteins are colloidal substances constituting the nitrogenous elements of animal and vegetable tissues. On digestion, they are converted in the stomach, by the action of the enzyme Pepsin, to Proteoses and Peptones; and then on further hydrolysis in the intestine, in presence of Trypsin and Erepsin, to Amino Acids. Some of the Amino Acids are absolutely essential for the building up of tissue. It is stated that kidney, liver and milk proteins are of unusual value. On the other hand, some, for example, Gelatin and Zein of Maize, do not yield all the important Amino Acids, and therefore, although serving as spacers of protein, they are incomplete as tissue-builders.

The Amino Acids not required by the system are broken up by the liver cells, the Nitrogen being excreted as Urea, Creatinin, Uric Acid, etc., and the balance of the molecule converted into Glycogen or neutral fats.

Fats are converted into Glycerol and fatty acids by the enzyme Lipase derived from the stomach and pancreas, the action being facilitated in the intestine by the emulsifying power of the bile. The products of digestion are absorbed by the cells covering the villi in the small intestine and are passed on as neutral fats by the lacteal system to the blood. They are then stored in the tissues or oxidised to produce heat and energy.

Carbohydrates may be classified as

- (1) MONOSACCHARIDES of the formula $C_6H_{12}O_6$ (Glucose, Galactose, Fructose, etc.).
- (2) DISACCHARIDES ($C_{12}H_{22}O_{11}$) include Saccharose, Maltose, Lactose.
- (3) POLYSACCHARIDES include Starch, Cellulose, Glycogen and Dextrin.

During digestion the carbohydrates are hydrolised by appropriate enzymes and are finally absorbed as Glucose and Levulose. These are **converted to Glycogen by the action of Insulin**, and this starch is stored in the tissues to be gradually liberated when required, furnishing heat and energy by oxidation. If excess of carbohydrates is assimilated it is synthesised into neutral fats and stored as such.

Inorganic Salts. Complete deprivation results in the death of the individual within a month. The following elements, in addition, to Carbon, Hydrogen, Nitrogen and Oxygen, enter into the composition of the tissues: Calcium, Potassium, Sodium, Magnesium, Phosphorus, Sulphur, Iron, Chlorine, and Iodine. Traces of Silicon and Fluorine are present in the bones and teeth. Cereal foods and tubers are lacking in Sodium, Phosphorus, Calcium, and Chlorine. Meat is rich in Phosphorus. Leafy green vegetables, most fruits, and milk, supply salts, but the latter is deficient in Iron.

In addition to **Vitamins** the **endocrine secretions** excite and control metabolic activity and therefore the vital processes of the organism.

Errors of diet, and especially the ingestion of **excessive quantities of carbohydrates**, with the probability of accompanying gastric fermentation, are thought to be predisposing factors in such diseases as pellagra, sprue, tuberculosis, nephritis, calculi, arteriosclerosis and diabetes. Cancer has been found to be preceded by digestive and other disturbances usually met with in people using an excessive carbohydrate diet.

Sucrose taken in large amount with a meal is especially prone to fermentation, with the production and absorption of irritating organic acids and toxic products. Abundance of carbohydrate also usually implies a deficiency in mineral salts and Vitamins.

The ordering of a properly-balanced diet, with a full recognition of the patient's idiosyncrasies, is one of the fundamental steps in the treatment of any organic disease.—W. E. Deeks, *Am. Jl. Trop. Med.*, May, '27, 111.

DIABETICS may eat large amounts of vegetables and fruit. New figures.—R. D. Lawrence and R. A. McCance, *B.M.J.* ii/29, 241.

(i) Proteins.

Biuret Reaction.

This reaction is one of several general reactions for proteins.

To obtain good results with the test in the recognition of Protein, the test solutions of Albumin, Copper Sulphate and Sodium Hydrate are best of following strengths:—Albumin in Distilled water 0.2%, Sodium Hydrate 1 Gm. in 10 Cc., and Copper Sulphate 5 Gm. to 100 Cc. water.

It is used to recognise Urea, which, heated in a capillary tube until the melted Urea is distinctly turbid and dissolved on cooling in water with a few drops of Soda Solution added, gives, on adding a drop of dilute Copper Sulphate Solution, a red to violet colour, which turns to blue on further addition.

Amino-Acids. *Syn.* AMIDO-ACIDS.—The hydrolysis of Proteins gives the amino-acids glycocoll, alanin, leucin, etc. Fischer, starting with glycocoll, synthesised 100 bodies closely allied to peptones,—he designated them 'polypeptides'—the work gave biology a clearer insight into the chemistry of animal and plant life.

These organic acids contain the Amino (NH_2) group. It has been suggested that all proteins are derived from Aspartic Aldehyde by condensation. They are both basic and acidic, *e.g.*, the following:—

Carbamic Acid NH_2COOH . (Amino-formic Acid.)

Glycocoll $\text{NH}_2\text{CH}_2\text{COOH}$. (Amino-acetic Acid.)

Sarkosin $\text{CH}_3\text{NHCH}_2\text{COOH}$. (Methyl-glycocoll.)

Alanin $\text{CH}_3\text{NHCH}_2\text{COOH}$. (Amino-propionic Acid.)

Leucin $\text{CH}_3(\text{CH}_2)_2\text{CH}(\text{NH}_2)\text{COOH}$. (Amino-caproic Acid.)

Aspartic Acid $\text{HOOCCH}_2\text{CH}(\text{NH}_2)\text{COOH}$. (Amino-succinic Acid.)

Glutarminic Acid $\text{HOOC}(\text{CH}_2)_2\text{CH}(\text{NH}_2)\text{COOH}$. (Amino-glutaric Acid.)

Tyrosin $\text{HO.C}_6\text{H}_4\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$. (Hydroxyphenyl-amino-propionic Acid.)

Taurin $\text{NH}_2\text{CH}_2\text{CH}_2\text{SO}_3\text{H}$. (Amino-ethane-sulphonic Acid.)

Amino-Acid fractions of the protein molecule are occasional constituents of the excreta, *e.g.*, leucin, tyrosin, cystin, in which last the Sulphur of Proteins resides. From others the equally familiar excretory products, or products of putrefaction, are derived,—such as Indol from tryptophane, cadaverin from lysin, and putrescin from arginin.

For further data on Amino-Acids, see Vol. I., pp. 4-5.

Estimation of Amino-Acids in the Urine, vide *Analytical Memoranda*.

Quantitative determination of most amino-acids conducted by titration with Hydrochloric Acid with the amino-acid dissolved in 90-95% Acetone, using Naphthol-Red as indicator.—B.C.A., Sept. '28, 977.

The Amount of Protein food needed for the actual physiological want of the body is not more than half that ordinarily consumed by the average man. A diet of low protein value is generally recommended for a healthy man and for those suffering from arteriosclerosis. Man was not intended to be the carnivorous animal he has become. It is frequently stated also that one should reduce carbohydrate intake.

Excessive protein feeding as such is **not harmful to the kidneys**:—the damage done to them being due to lack of Vitamins in diet.—Work at St. Thos. Hosp., P.J. i./26,293.

Quality of Protein in Nutrition. Importance of biological values of proteins. Pellagra broke out among Armenian refugees in Port Said 1916. On improving diet it stopped. Meat has thrice the value of maize.—R. H. A. Plimmer, L. i./21,947.

Protein metabolism during starvation and after giving Milk protein.—L. i./14,236.

Edible protein and fat from Glucose, converted sawdust and Ammonium Phosphate.—B.M.J. i./22,115.

Diets, effects of various, and the resistance of animals to certain poisons.

The results of the experiments using **Acetonitrile** CH_3CN indicate that there are factors entering into the composition of foods, more complicated than its Protein, fat and carbo-hydrate composition, and suggest lines of research to find means of increasing resistance of the body to the poisons of disease. Hygienic Lab., Bulletin No. 69, June, 1910.—U.S. Public Health and Marine Hosp. Service, Washington, 1910, v. also B.M.J. ii./10,1270.

Acetonitrile as a test for thyroid and further feeding experiments.—P.J. i./14,534,599.

(ii) **Fats.** This group comprises the glycerides of a large variety of fatty acids, *e.g.*, Oleic, Palmitic, Stearic, etc. Mention may also be made of Lecithin (*q.v.* Vol. II.), which is an important constituent of eggs and various animal tissues, and the important group of substances known as **Sterols**, one of which is associated with Vitamin D. This Sterol is not apparently synthesised in the body and must be supplied in the food. The type of fatty acid present in the ingested fat is important; thus, fats such as Linseed Oil, containing highly unsaturated fatty acids have greater inhibitory effect on gastric secretion than fats like Olive Oil which contain more saturated fatty acids.

Fats formed from carbohydrates contain a larger proportion of Stearin and Palmitin, hence the firmness of the fat of cattle compared with that of omnivorous animals. In carbohydrate starvation oxidation of fat may be incomplete, and intermediate products, β -Oxybutyric Acid, Diacetic Acid, and Acetone, will pass into the blood and urine. Two ounces is usually considered the average daily allowance of fat for an adult.—S. J. Cowell, L. i./29,996.

(iii) **Carbohydrates.** (See Bread and Flour Control *postea*).

Importance of removing Carbohydrate matter from the teeth. Many organisms in the mouth ferment Carbohydrates producing chiefly Lactic Acid. MONOSACCHARIDES are the most readily fermented. DISACCHARIDES require to be first inverted to MONOSACCHARIDES by an enzyme formed by certain of the mouth organisms before Lactic Acid can be produced. STARCHES require a double inversion—the first stage brought about by ptyalin or organisms before fermentation to an acid can occur. 1 mol. $\text{C}_6\text{H}_{12}\text{O}_6$ (glucose) produces 2 mols. Lactic Acid; 1 mol. of the Disaccharide Cane Sugar $\text{C}_{12}\text{H}_{22}\text{O}_{11} + 1 \text{ mol. H}_2\text{O}$ gives 1 mol. each Dextrose and Lævulose, with ultimate formation of Lactic Acid; and the polysaccharide $(\text{C}_6\text{H}_{10}\text{O}_5)_n$ (Starch) + H_2O gives $\text{C}_6\text{H}_{10}\text{O}_5$ Dextrin + $\text{C}_{12}\text{H}_{22}\text{O}_{11}$ Maltose, which Maltose is converted into 2 mols. Dextrose, and ultimately to Lactic Acid. The Lactic Acid dissolves the lime salts of the enamel and a cavity is originated at the point of action.

(iv) **Mineral Salts.**

Iron enters into the elaboration of hæmoglobin and Iodine into Thyroxin, whilst the alkaline earths with Chlorine and Phosphorus control a constant osmotic pressure in the body. Calcium must be continually supplied in large quantities, as it is not only required in large amount but it is excreted even in the absence of intake and together with Iron and Iodine it may be deficient in the diet of mankind under certain conditions, symptoms of disease being thereby produced.—S. J. Cowell, L. i./29,997.

In TUBERCULOSIS, very high feeding often results in arrest of the disease. In urinary and renal diseases lime and foods containing lime are to be excluded. Preference for Magnesia bases to be given in treatment of oxaluria.

For Diabetic Foods, see Vol. I., p. 591.
Queer foods and 'faddists'.—Jl. Trop. Med., Apl. 2/23,113. See also Agar Seaweeds, etc., L. i./05,1524.

CALORIE VALUES OF FOODS.

The following figures (**Calories**) are usually given as the true worth to the body of the different nutritive constituents as sources of potential energy: Protein 4, Carbohydrates 4, Fat 9 Calories. Proteins and carbohydrates seem to be oxidized quickly in the tissues, fats more slowly. Therefore, if a rapid output of energy is required, the *first* group will be more serviceable, whereas a slow production over a long time will be equally well met by fat.

Method of Applying the Calorie Standard. Multiply the percentage of protein or carbohydrate (or both), that the food contains by 4.1 and the percentage of fat by 9.3 to obtain the total Calories yielded by 100 parts of the food in question.

Standard Nutritive Requirements. A healthy man of 150 lbs. requires food equivalent to 3,000 calories *e.g.*, the following: Protein 120 grammes, Carbohydrates 500 grammes, Fat 50 grammes. Such a standard may be regarded as suitable for a man of average build and weight, doing a moderate amount of muscular work; if a greater intake of energy is demanded it should be met by increasing the amount of fat consumed. A calorie (*i.e.*, a Kilo calorie) is the amount of heat necessary to raise a litre of water 1° C. or a lb. of water 4° F. The amount of food consumed varies in caloric value from 1,800 to 8,000 units.—W. E. Deeks, *Am. Jl. Trop. Med.*, May, '27.

The lack of fat is a serious matter when preserved meat is used. The proportion of fat to meat in fresh meat is about 1 to 4, but in corned beef this is reduced to 1 to 10. A good form of fat ration is cheese, but lard or suet are also suitable.

The criteria of an efficient diet.—Sir F. Gowland Hopkins, *Pr.*, Mar., '26, 214.

Calorie Values in Army Rations. The recruit who is a growing lad requires more food than the trained adult soldier and during the war it was recommended that young recruits should receive food representing an extra 200 calories per day over the ordinary ration, receiving a diet representing not less than 3,750 calories per day. The present Army peace ration is 3,600 calories, while for an army in the field a diet containing 4,000 calories is needed, and for men on lines of communication 3,350 is sufficient. Lemon juice made from fresh lemons now substituted for lime juice in our Army.—Sir W. Beveridge, *Pr.*, Mar., '26, 181-6.

Calorie Values (Kilo calories) of a few common foods.

Milk 0.70.	Coarse White Bread 3.03.
Potatoes 0.98.	Fat Beef 3.27.
Lean Beef 0.98.	Peas 3.31.
Eggs 1.59.	Lentil Flour 3.55.
Cheese 2.4.	Fat Mutton 4.03.
Fine Wheat Bread 2.74.	Butter 8.60.
Wholemeal Bread 2.78.	Bacon 8.86.

—Hutchison's Food and Principles of Dietetics.

Apples, fresh 0.53	Cream 2.07.
Bananas, without skin 0.80	Dates, dried 3.30
Cabbage	Fish 1.10
Cauliflower	Grapes 0.66
Carrots	Margarine 7.50
Onions	Rabbit 2.9
Turnips	Rice, boiled 0.93.
Chicken 1.40.	Tomatoes 0.17.

—U.C.H., 1926.

The above Calorie Values are calculated from the percentage composition and represent the *kilo calories* yielded by complete combustion of 1 Gm. of each food.

One pound of **Raisins** contains 1,635 food units of energy, the same as three dozen **Eggs**. One pound of **Beans** contain less than half as much food value, one pound of **Peas** less than one third, one pound of **Potatoes** and one pound of **Milk** together fall 925 points short. Even one pound of **Beef** fails to equal it by 1,055 food units.—'A Patriot,' *P.J.I.*/15,825,886.

Horlick's Malted Milk Lunch Tablets. Total large calorie value of a bottle probably about 450. The following figures were obtained, but they do not include all:—

Protein from total Nitrogen	15.4 Gm.	×	4.1 =	63.1
Fat	7.8 Gm.	×	9.3 =	72.5
Reducing Sugars	59.7 Gm.	×	4.1 =	244.8

(Abstd., B.M.J. i./16,345).

330.4

Calorie Values of some proprietary food preparations. See B.M.J. i./10,1239.

Yeast Extracts as Food.

Yeast Extracts, providing they are correctly labelled, may be quite good and wholesome in their way. They are practically identical in composition with Meat Extracts and similar in taste. Their presence in Meat Extracts can sometimes be determined microscopically by observing yeast cells. Diluted Fehling's Solution on being brought to the boil after adding a quantity of the Aqueous Solution of the extract to be examined shows a bulky curdled precipitate of greenish grey colour if yeast extract be present.

Nucleic Acid of Yeast compared in its chemistry with Thymus-Nucleic Acid. The resemblance between Nucleic Acids and **Phosphatides**.—Abst. Ann.Rep.Chem.Soc.1919 (Vol. XV.) p. 157.

ACCESSORY FOOD FACTORS. VITAMINS.

Much work has been done on the Accessory Food Factors since we issued the last edition of Vol. II., and we outline in the following pages the extent of investigations by leading authorities, with their conclusions up to date. Whilst not wishing to minimise the importance of the subject, we are inclined to think that a certain amount of the *early* Vitamin work must have been completely erroneous, and that a great deal that is now accepted as fact will have to be revised in the light of subsequent knowledge. A selection of 'general' information relative to the matter is given, followed by an alphabetical classification of the Vitamins from 'A' to 'E.' The production of Vitamin 'D' by the irradiation of Ergosterol is dealt with on p. 104, and forms one of the most important additions to this chapter.

Vol. I., p. 592, should also be consulted.

Vitamins in General.

The current classification of Vitamins (Prof. A. J. Clark, P.J.ii./28,518) may be given thus:—

FAT-SOLUBLE:

- A. Anti-infective.
- D. Anti-rachitic.
- E. Reproductive.

WATER-SOLUBLE:

- B₁ Anti-neuritic.
- B₂ Anti-pellagra.
- C. Anti-scorbutic.

The harm done by wrong feeding in the past can never be entirely repaired by belated attention to the need for Vitamins, but the use of Vitamin-containing foods may prevent the damage from getting worse.—R.H.A. Plimmer, Pr., Mar., '26,232-248.

Food and the Public Health. The diet of the poor—white bread, margarine, skimmed milk, cheese, and tinned meat, **cannot maintain vigour sufficient to ensure an adequate output of labour or resistance to attacks of illness**.—W. J. Howarth, Pr., Mar., '26,188.

This country spends £500,000,000 a year on imported food. These products may be deficient in vital principles.

—W. E. Elliott, B.M.J. ii./23,199. *We believe they are.*

The Danish peasants' diet of 50 years ago, mainly consisting of dairy produce and vegetables was the most healthy and by far the cheapest.—M. Hindhede, Pr., Mar., '26,260.

Diet in Public Schools. Allowance of butter should not be less than $1\frac{1}{2}$ oz. per day and of milk $\frac{3}{4}$ pint, with fresh fruit daily and stone-ground flour (80 %) made compulsory.—L. R. Lemprière, Pr., Mar., '26,204.

Diet of whole wheat, milk, sprouted legumes, far surpasses one of white bread, tea, sugar, and margarine.—R. McCarrison, B.M.J. ii./26,730.

Bone Marrow changes. Effect of deficiencies of Vitamins.—G. M. Findlay, B.M.J., i./25,359.

Following a diet deficient in Vitamins or Phosphorus, the blood of rats shows a distinct reduction in bactericidal activity to *Staphylococcus aureus*.—G. M. Findlay and I. Maclean, Jl. Biol. Chem., XIX., p. 63; C. & D. i./25,453.

While in Greenland, where the natives subsist exclusively on fish and meat, scurvy and rickets are unknown, in Labrador, where civilisation has trained the natives to buy cereals and dried and canned provisions, both diseases are universal. Possibly fish and fish-eating animals contain much Vitamin 'C,' as well as 'A,' in their tissues, derived from marine vegetation.—L. i./27,1358.

For a recent Résumé on Vitamins, see R. R. Bennett, P.J. ii./28,79, *et seq.*

Man and most other animals cannot synthesize Vitamins—they must be taken from food, either animal or vegetable. Lack of them means lack of stability of the nervous system, resulting in irritability, excitement, fear, anger, and other mental disturbances.—W. E. Deeks, Am. Jl. Trop. Med., May, '27.

International Standards of Vitamins 'B,' 'C,' and 'E' are needed.—K. H. Coward, P.J. ii./28,575.

Water Cress.—Remarkably **rich in Vitamin 'A'**; 0.1 Gm. of green leaf promotes normal growth in rat. Also contains small amount of Vitamin 'D.' Growth-promoting properties stronger in spring and summer. Very rich in Vitamin 'C'; 1 Gm. daily protects guinea-pigs for 70 days.—K. H. Coward and P. Eggleton, L. i./28,98. (We incline to the view—by instinct—that the early spring growth is far richer than the later.)

VITAMIN "A"

Reactions of Vitamin 'A' (Qualitative).

Arsenic Chloride Test (Rosenheim and Drummond) for Detection of Vitamins in Oils.

Add a drop of the oil to Arsenic Chloride 1 Cc., shake gently. A blue colour will appear in the Arsenic Chloride if Vitamins are present. The colour is not permanent.

We have tried numerous oils with the method :—

Almond Oil.

Linsced Oil.

Cod Liver Oil.

Olive Oil.

Egg Oil.

Castor Oil.

Sesame Oil.

Soya Bean Oil.

but a positive result was only obtained with Cod Liver Oil.

Antimony Trichloride (SbCl_3) 20 % in Chloroform gives a colour not quite so definite as the Arsenic Chloride colour, but the reaction is possibly more sensitive. 2 Cc. of the solution is added to a solution of the Oil in Chloroform.

Cod Liver Oil exposed to the air for a few hours does not respond well with Arsenic Chloride, due no doubt to oxidation.

Arsenic Chloride, Methyl Sulphate, Trichloroacetic Acid, Acetyl and Benzoyl Chloride, give a blue colour with substances containing Vitamin 'A.' Reaction is very sensitive and persists sufficiently long to enable a colorimetric comparison with a suitable standard. A definite parallelism between intensity of colour and growth-promoting property of a number of oils and fats was observed. Irradiated active Cholesterol did not react with Arsenic Chloride.—O. Rosenheim and J. C. Drummond, Biochem. Jl., '25,19, p. 753; J.C.S., Ai./25,1515.

Rosenheim's Test thought specific.—L. ii./26,806.

Quantitative estimation of Vitamin 'A' in Cod Liver Oil. Sir F. Gowland Hopkins and Harriette Chick reported to the League of Nations Health Organisation (Report of Accessory Food Factors Committee) on the estimation of Vitamin 'A' in Cod Liver Oil, *re* the validity of the method of Rosenheim and Drummond in comparison with the biological method. The colour intensity (blue) in using the above methods is measured against standard glasses in a **Lovibond Tintometer**. The method drawn up in 1925 by Prof. Poulsson for the biological assay of Vitamin 'A' is defective in that no provision was made for an adequate supply of Vitamin 'D' to the animals during the period of the test; the method chosen by the investigators included the administration of excess of anti-rachitic Vitamin during the latter part or the whole of the pre-observation period. The Vitamin 'A' values of the seven oils as determined by the workers using the biological test came out in roughly the same order. The colorimetric method affords information consistent with that derived from the biological tests, but tests should be made with other substances containing Vitamin 'A,' *e.g.*, butter and palm oil, before concluding it is generally valid.—L. i./28,148.

Vitamin 'A' does not appear to be identical with Chlorophyll A or B, Carotin or Xanthophyll, but these should be removed from foodstuffs and natural products by shaking a Petroleum Ether solution with Norite 10 Gm. to 100 Gm. of butter, fat, etc.

While Vitamin 'D' does not qualitatively interfere with the colours for A, Olive Oil and Oleic Acid appear to inhibit.

An Acetone-Ether extract of **early spring spinach** is a highly potent source of Vitamin 'A,' measured either by feeding or by colour tests. Cod Liver Oils subjected to irradiation and aeration failed to respond to tests for Vitamin 'A.'—S. G. Willimott and F. Wokes, L. ii./27,8; 143,305.

Search for colour reactions of Vitamin 'A.' The Antimony Trichloride colour test is unaffected by moisture, and hence special precautions are not needed.—H. T. Cocking and E. A. Price, P.J. ii./26,175; C.D. ii./26,246; See also J. R. Walmsley, P.J. i./26,73.

Detection and estimation of Vitamins 'A' & 'D' in Cod Liver Oil and various food products.—F. Wokes and S. G. Willimott, P.J. ii./25,718; ii./26,473,495,521,571; i./27,752.

Comparative experiments showed that there is **no agreement** between the Antimony Trichloride test (Carr and Price, B.C.A., '26,A870) and feeding tests with young rats. **Whale Oil** gives the colour reactions, but does not prevent avitaminosis with rats on Vitamin 'A' deficient diet. Doubt is expressed whether the colour is due to Vitamin 'A.'—B.C.A., '28,A925.

Some hold, however, that the **Antimony Test runs nearly parallel with the Biological Test** for Vitamins. The matter is being investigated, and it is probable that either this or the Arsenic Test **may do away with the Biological Test.**—K. Coward, P.J. ii./28,575.

U.S.X. method (optional) cannot be regarded as satisfactory and occupies 10-12 weeks. It is based on the estimation of the minimum amount of oil necessary to meet specific growth-promoting requirements in standard test-animals, *i.e.*, albino rats. The results are given in units. The colour test is easily carried out but its efficacy is doubted.—F. H. Carr, C.D., Dec., 18/26.

Cod Liver Oil extracted from a twenty-three year old Malt and Oil emulsion gave a colour test of about 250 units, showing that these emulsions retain their Vitamin 'A' for considerable periods (a Norwegian oil of good quality contains on an average about 500 units of Vitamin 'A' per Gm.).—J. M. Jones, P.J. ii./28,91.

In the cod, Vitamin A is not confined to the liver, but, in the period preceding spawning, is found in considerable concentration in the roe, both hard and soft.—Spec. Report, Med. Res. Council, L. i./24,364.

Vitamin A content of **Maize Oil** high, comparing favourably with Palm Oil and winter Butter Fat. Neither Linseed nor Arachis Oil any good as source of Vitamin A.—A. D. Stammers, L. ii./24,598.

Oil of Cloves contains an antirachitic Vitamin. Oils of Sandalwood, Lemon, Orange and Fennel Seed had no antirachitic effect.—P. G. Shipley, E. M. Kinney and E. V. McCollum, Jl. Biol. Chem., '24,59,177; P.R. '24,188.

To diminish the buffer substances of cow's milk, which render much of the

gastric secretion of the stomach inactive, the following formula is recommended: Milk 24 ounces (710 Cc.), Water 12 ounces (355 Cc.), Sucrose $\frac{1}{2}$ ounce (15 Gm.), Lemon Juice 21 Cc. This is well tolerated by infants. To secure adequate anti-rachitic elements in infants' diet the addition of one egg yolk to a quart of milk is of decided value. The egg yolk added to milk acidified by lemon juice ensures a food rich in Vitamins A and C, which is easily assimilated by delicate children.—A. E. Hess and M. J. Matzner, J.A.M.A., May 17/24, per B.M.J. ii./24,118.

The production of Vitamin A in plants, though dependent on light, is independent of Carbon Dioxide, Oxygen and Chlorophyll. In the animal, its physiological function appears to be related to the metabolism of fats, Calcium and Phosphorus.—Med. Res. Council. Report on Vitamins.—B.M.J. i./24,332.

According to Drummond and others the Vitamin-active material in Cod Liver Oil is represented by not more than 10%, and probably a good deal less, of the unsaponifiable fraction from the active oil. The amount of active substance needed to enable a young rat of 100 Gm. weight to grow is perhaps 2/1,000,000 Gm. per diem.—P.J. i./26,292.

1/200 milligramme of active fraction from Vitamin 'A' maintains a rat in health.—J. C. Drummond, L. i./26,272.

Vitamin 'A' as an Anti-infective Agent.

Experience in nutritional work suggests that Vitamin 'A' is more directly related to resistance to infection than any other food factor, and although the specificity of this Vitamin and infection is not settled the evidence obtained is in its favour. Vitamin 'A' plays an important part in conferring resistance to many types of infection—puerperal septicæmias and acute rheumatism may be related to Vitamin 'A' deficiency. Although Vitamin 'D' controls the calcification of bones and teeth it has no direct power to promote resistance to infection and if a substitute for Cod Liver Oil is given it ought to be at least as powerful as this oil in content of both Vitamins 'A' and 'D'.—H. N. Green and E. Mellanby, B.M.J. ii./28,695.

In the absence of Vitamin 'A' the epithelial linings of all parts of the body show degeneration, and become an easy prey to invading organisms. A trace of Hydroquinone renders it relatively stable.—K. H. Coward, P.J. ii./28,572.

Stability.

PASTEURISATION (heating to 145 or 150° F. for $\frac{1}{2}$ hour) has practically no effect on Vitamins A and B, which have relatively high resistance to heat.—J. M. Hamill, Ministry of Health Report, L. ii./23,339.

While the Vitamin in butter is not diminished by exposure to 120° C. for 4 hours, it is in the same period greatly diminished, and in 12 hours completely destroyed, if the butter is thoroughly aerated during the heating, *i.e.* one must conclude that, though fairly resistant to heat, this Vitamin is readily destroyed by oxidation.—B.M.J. i./21,237; i./22,236. Heating at 120° C. and 32 hours aeration destroys it.—E. Mellanby, B.M.J. i./24,895.

Ozone, even in the dark, destroys Vitamin 'A'.—S. S. Zilva, B.M.J. i./25, 1110.

Exposure of Cod Liver Oil to any source of white light of sufficient intensity results in 'delumination'—disappearance of normal golden fluorescence—and destruction of Vitamin 'A'. Kept for some months in dark it regains much of its fluorescence but Vitamin 'A' is permanently destroyed.—P. R. Peacock, L. ii./26,329.

Experiments with rats indicate some connection between deficiency in Vitamin 'A' and formation of phosphatic calculi.—Prof. E. C. van Leersum, B.M.A. 1927, per B.M.J. ii./27,874.

Gastric lesions occurred in rats fed on synthetic diets in which the only deficiency was want of Vitamin A.—Pappenheimer and Larimore, quoted by McCarrison, B.M.J. i./25,359.

Relative content of Vitamins 'A' and 'D' in Cod Liver Oil. The ash content of bones of nearly 200 rats showed that the Vitamin 'A' content in Cod Liver Oil bears no necessary relationship to that of Vitamin 'D'. The medicinal worth of Cod Liver Oil depends more on its anti-rachitic value than upon its Vitamin-A content. If the amount of one of these Vitamins in a particular oil bears no relationship to the other, the biological method of testing in the U.S.P., which aims at the assay only of Vitamin 'A', is open to criticism.—J. L. L. Clare and K. M. Soames, L. i./28,150.

The sexual condition of the cod during spawning does not influence the Vitamin 'A' content of the oil.—E. Poulsson, L. ii./28,479.

***Advita.** (T.M. 478190). A concentration of Vitamins 'A' and 'D' of potency 50 times the minimum for Cod Liver Oil U.S.

***Essogen.** (T.M. 477726). A preparation of similar type 10 times the U.S. Cod Liver Oil strength.

VITAMIN "B"

Stability of Vitamin 'B.' Jansen found that 'paddy' of over 100 years old, kept in storehouses in Java, was still almost as rich in anti-beri-beri vitamin as fresh rice.—Trans. Roy. Soc. Trop. Med., Vol. 17, No. 4, p. 237.

Extreme heat and undue alkalinity are unfavourable to its preservation, and on both sides of neutrality the rate of destruction by heating was a function of the pH of the medium in which it was dissolved.—Jl. A.M.A. i./27,407.

Vitamin 'B' content of seeds may diminish somewhat with lapse of time, but diminution is not great. Seeds which have lost power of germination have not necessarily lost Vitamin 'B' content. Experiments with 38-year old lentils and peas.—B.M.J.E. i./24,24.

The antineuritic food factor is completely destroyed by exposing a layer, 2—3 mm. deep, of aqueous yeast extract for a few hours to radiation from a quartz-mercury lamp.—J.C.S., Ai./25,751.

Marmite 8% corresponds to 4% of Dried Yeast, as tested in pigeons.—per C.D. ii./27,387.

Bread, nutritive value of, in reference to Vitamin content.
—see Brcad Chapter.

The Dual Nature of Vitamin 'B.' Two factors are concerned, one the *anti-paralysis*, and the other independent of this and concerned with *digestive* processes. The separation is effected by extracting rice polishings with 4 times their weight of Acetic Acid (1%) for 8 hours at 40° C. After filtering and evaporating *in vacuo* to a 1 in 1 extract, this is treated with Lead Acetate. The Lead is removed from the filtrate by precipitation with Sulphuretted Hydrogen, and the liquor evaporated *in vacuo*. The filtrate causes polyneuritis, but the precipitate portion, while ensuring maintenance of health and growth, will not prevent polyneuritis. On the other hand, it relieves, by causing rapid evacuation of the bowel, the characteristic bowel 'stoppage' in pigeons suffering from Vitamin 'B' deficiency.—J. L. Rosedale, Biochem. Jl., XXI., 6,1267.

The anti-beri-beri substance, 'B₁' (as distinct from Vitamin 'B₂' or 'PP', the anti-pellagra Vitamin) has been isolated by Jansen and Donath from rice polishings and has the formula C₆H₁₀ON₂. One part in 500,000 considered as preventive of beri-beri in man.

A difference between Vitamin 'B' and Vitamin 'PP' is that the former is destroyed by heating with alkali, while the latter is not. To distinguish between the two, the Medical Research Council (Vitamin Committee) has proposed that the anti-neuritic substance be called 'B₁' and the anti-pellagra substance 'B₂'.

The existence of Vitamins as definite chemical substances can no longer be denied. Scepticism can now only be attributed to ignorance and prejudice.—R. H. A. Plimmer, Pr., July '28,24. See also L. i./27,833.

Hunt (1928) postulates the existence of a third member of the B complex. Marrian and Co-workers found they could get the retraction of the neck of pigeons characteristic of B deficiency in animals receiving B (Marmite) in abundance, but which otherwise received *no* food. Hence, the influence of B on these symptoms is not a direct one but an indirect one somehow through the food consumed. Dried Yeast contains B₁ and B₂ in proportion of 1:7.5. Silica gel absorbs the B₂ preferentially.—K. H. Coward, P.J. ii./28,572.

B₁ and B₂ in yeast.—B.C.A. '28,A556.
Wheat or maize are relatively rich in Vitamin 'B₁' and poor in Vitamin 'B₂'.—B.C.A. '28,A926.

Prof. R. H. A. Plimmer found in animal experiments (pigeons) that the following percentages of varying foodstuffs were needed in the diet to provide an adequate amount of Vitamin 'B':

Whole meal..	.. 75%	Bran (Middlings) ..	30%
Rye 55%	Wheat Germ..	.. 10%
Whole Barley 65%	Yeast Extract 10%
Oatmeal 95%	Potatoes 90%

—B.M.J. i./26,239.

Taking Dried Yeast as 100, the relative Vitamin 'B' content of various cereals is as follows: Wheat Germ 66, Bran 12—13, Middlings 12—13, Whole Wheat 8—10, Rye, Millet, Dari, Maize, Barley 7—9, Buckwheat 5—6, Oatmeal 4, White Rice and White Flour nil.—C.D. ii./27,811.

Fresh lemon rind contains appreciable amounts of 'B'.—S. G. Willimott, *Biochem. Jl.*, No. 1, '26,31.

FUNCTION OF THE LYMPHOCYTE AND OF LYMPHOID TISSUE IN NUTRITION. When a rat is kept on a diet free from Vitamins the animal dies. There is a profound atrophy of lymphoid tissue—obvious to the naked eye. The lymphocyte has an important and specific function in maintaining nutrition. The disturbances in nutrition which follow the withholding of Vitamin B are secondary to a specific lesion which leads to an interference of the functional activity of the lymphoid tissues. Absence of the Fat Soluble A Vitamin does not lead to atrophy of lymphoid tissue and there is no lymphopænia. Vitamin B is necessary for life, not because it is necessary for all the cells of the animal, but because it is needed for normality of lymphoid tissue.—W. Cramer and Co-workers, *L. ii./21,1202*.

VITAMIN B AND APPETITE. *Palm-kernel Oil* heated 4 hours at 160° C. and subsequently treated with super-heated steam at 230° C. is quite free from Fat Soluble A Vitamin, used as a source of fat in rat experiments. The animals were first fed on a basal ration containing Vitamins A and B in the form of Cod Liver Oil and Marmite respectively. Results showed the Vitamin B acts by facilitating the efficient carrying out of the functions of the intestinal canal.—S. Wright, *L. ii./21,1208*.

MODE OF ACTION OF VITAMIN B. The digestive tract is the key to the problem. The functional integrity of the digestive tract is dependent on presence of substances with specific drug-like actions. One group (Water Soluble Vitamin B) has a specific effect on lymphoid tissue. The other (Fat Soluble Vitamin A) has a stimulating effect on the intestinal mucous membrane and directly, or indirectly, on the formation of blood platelets.—W. Cramer, *L. i./23,1046*. See also *Vol. I.*, page 595.

Ⓟ***Metatone** (T.M.490271). A general tonic and is stated to contain in each fluid ounce Vitamin 'B' Extract 10 grains, Nucleinic Acid 2 grains, Calcium and Potassium Glycerophosphate of each 4 grains, Sodium Glycerophosphate 2 grains, Manganese Glycerophosphate $\frac{1}{2}$ grain, Strychnine Glycerophosphate 8/200 grain. *Dose*.—1—4 drachms.

For a further consideration of Vitamins in relation to Beri-Beri—especially with regard to the earlier work—see Beri-Beri, Vol. II.

VITAMIN " C "

Destruction of Vitamin C by heat.

A greater destruction of Vitamin C, present in fresh milk, occurs when heated to 60° C. for $\frac{1}{2}$ hour than when boiled for a minute. Vitamins are destroyed much more easily in alkaline than in acid fluid—it need be only feebly acid. Prolonged boiling, as in making stews, destroys nearly the whole of Vitamin C in vegetables. Zilva found that this Vitamin was completely destroyed by boiling one hour in presence of Oxygen, but no destruction occurred when it was boiled two hours in an atmosphere of Carbon Dioxide.

Lime Juice has only a quarter the Vitamin C content of **Lemon Juice**. The simplest way of transporting Vitamin C is by use of **Dried Peas**. They contain little Vitamin when dry, but produce large quantities when allowed **to germinate**. Germinating seeds contain large amounts of 'B' and 'C.'

Pasteurisation of Milk at 145° F. for 30 minutes weakens Vitamin C.—J. M. Hamill, Ministry of Health, *L. ii./23,339*.

Vitamin 'C' content of cow's milk diminished by Pasteurization. Half an hour at 63° C. is worse than quarter of an hour at 85° C. A rapid heating of Pasteurized milk to boiling point does not impair it any more.—per *Jl. A.M.A.* ii./25,2002.

In *Dried Milk* there is a risk of losing the 'C' factor.—B.M.J. i./25,580.

Aeration (bubbling air through) of an antiscorbutic solution (Lemon Juice deprived of acids) inactivated it. Boiling an active solution 2 hours in an atmosphere of CO_2 , on the other hand, caused no diminution, but boiling 1 hour with aeration caused almost complete loss. The fat soluble factor behaves similarly. The antineurotic factor is more stable towards oxidation, e.g. ozone.—S. S. Zilva, L. i./21,478. See also A. F. Ness, *ibid* 938.

Lemon juice can be decitrated, concentrated and kept *in vacuo* for 6 months without loss of Vitamin C.—B.M.J. i./24,720. It is present in Cort. Limonis. It can be concentrated to 0.03% of lemon juice. The molecule is not larger than that of a hexose.—Prof. Drummond.

Experimental scurvy. Comparative value of South African foodstuffs. Vitamin content of diet for native workers on the Rand mines to be kept high. Vitamin C to be supplied by oranges, pineapples and naartjes in season. Vegetable rations not to be given after too long cooking.—E. Marion Delf, L. i./22,576.

Scurvy is not simply due to lack of fresh food, as Prof. Mouriquand holds. It can be prevented or cured by the juice of Citrus fruit which has been preserved for more than a year.—B.M.J. i./23,195.

Ferrier Deep beer, in South Africa, which is fermented for only 2-3 hours, contains as much Vitamin C as fresh English dairy milk.—E. M. Delf, T.D.B., Vol. 19., 1922,764.

Potatoes, antiscorbutic properties of. Experiments with guinea-pigs showed that fresh, raw, peeled potatoes were equal to cabbage and dandelion in antiscorbutic value. Pounded potatoes or extracted juice no use.—Bezssonof, per JI. Trop. Med., Oct. 16/22,332.

Lister Institute has devised a method of keeping the antiscorbutic factor for 5 months.—P.J. i./25,77.

The antiscorbutic Vitamin of Orange Juice, desiccated without heat, found to be soluble in 80 to 95% Ethyl and Methyl Alcohol. The solution protected animals from scurvy. Being insoluble in Butyl Alcohol, Petroleum Ether, Acetone, Ether, Chloroform and Ethyl Acetate indicates that the Vitamin is neither a fat nor a lipin.—E. B. Hart and Co-workers, JI. Biol. Chem., 1922, per T.D.B. 20/23,398.

Antiscorbutic value of Oriental fruits and vegetables. As a result of experiments on guinea-pigs, pomelo, cucumber, chico and guava were found to afford the best protection from scurvy.—H. Embrey, JI. Trop. Med., May 1/23,144.

Orange Juice supplied to the Navy has to be tested for 'C,'—P.J.ii./28,580.

Rats and prairie dogs apparently have the power to synthesize this Vitamin and naturally never suffer from scurvy. The rat is regarded as not requiring it. If canned vegetables and fruit are sealed before being subjected to heat, thus reducing oxidation, all the Vitamins are fully preserved.

Potatoes found experimentally to be antiscorbutic, but as ordinarily prepared for table have little value. Raw or undercooked meat will heal. The problem is not yet solved.—F. C. B. Gittings, B.M.J i./25,483.

VITAMIN " D "

Vitamin 'D' produced by prolonged exposure of Cholesterol to Ultra-Violet light, which forms a semi-solid waxy material with intense antirachitic action.—Prof. J. C. Drummond, B.M.J. i./26,239.

The supply of Vitamin 'D' comes from **animal fats** but ultimately all Vitamin 'D' comes from irradiation of Ergosterol in the skin, either of an animal or of a human being. In high latitudes very little ultra-violet light reaches the earth in winter, and practically none reaches those who dwell in **smoky towns**. Hence, there is every reason why **dwellers in Northern towns should suffer from Vitamin 'D' deficiency in winter**. They cannot make it themselves, and **most of the animal fats** they get are **from animals who have received little ultra-violet irradiation**. Margarine firms are taking steps to introduce Vitamin 'D' into their products.—Prof. A. J. Clark, P.J. ii./28,518.

Rosenheim and Webster, *cf.* L. i./27,307, found that **only the protoplasmic Sterols can be activated** by Quartz-lamp irradiation, excretory ones cannot, and both the secondary Alcohol group and the unsaturated Carbon linkage in the Sterol molecule must be intact for activation

Further work showed that it is **not the Cholesterol that is activated but an impurity in it.** (Cf. B.M.J. i./27,296.) The **provitamin is a Sterol of an unsaturated and labile type of which Ergosterol is the only known representative.** The amount of Ergosterol in ordinarily pure Cholesterol is about 1 in 2000. It was found that a daily dose of 1/10,000 mgr. of irradiated Ergosterol cures and prevents rickets in rats given a rachitogenic diet. It was found also that the band 247 $\mu\mu$ in irradiating is characteristic of Vitamin 'D.' Some of the rays were found to have destructive effect. Vita Glass cuts off rays below 260 $\mu\mu$ and hence may let through the needed rays, but this is not confirmed. Some contend that Ergosterol is not the only precursor of Vitamin 'D.'

Hypervitaminosis. Bad effects only likely from doses 100,000 times the quantity needed to cure really florid rickets.

There is no known colour test specific for Vitamin 'D.'—K. H. Coward, P.J. ii./28,572.

The content of Vitamin 'A' in Cod Liver Oil, as previously mentioned, bears no necessary relation to that of Vitamin 'D.'—J. L. L. Clare and K. M. Soames, L. i./28,151.

Stability. The antirachitic Vitamin in Cod Liver Oil is not destroyed by Hydrogen Peroxide, Hydrogen Sulphide, Sulphur Dioxide, or Formaldehyde Solution, but is readily destroyed by Nitrous fumes, and slowly by direct steam or contact with mineral acids.—Jl. Biol. Chem., per Jl. A.M.A. ii./25,224.

Vitamin 'D' is not destroyed at 115° C. for 1½ hours, but is largely destroyed in 1 hour at 100° C. in N/10 acid or alkali.—B.C.A., Dec. '28,1405.

Estimation of Ergosterol

Ergosterol made with Yeast gives, with **Antimony Trichloride**, blue colours very similar to the 'Vitamin' colours given by the same reagent on Cod Liver Oil. Quantitative estimation by the *Lovibond Tintometer* showed the tint produced to run parallel with the concentration of Ergosterol.—F. Wokes and S. G. Willimott, Qtrly. Jl. Pharm., Vol. I., No. 2, 188.

Quantitative Estimation Vitamin 'D.'

There are two units of antirachitic potency at present in use:

1. The **Coward unit** (Coward, Q. J. of P., '28, 1, 27) represents the amount of activity contained in 1/10,000 mgr. of a standard preparation of irradiated ergosterol.
2. The unit of Jephcott & Bacharach, Biochem. Jl. '26, 20, 1351; '28, 22, 60), which is identical with the Ostelin unit, *i.e.*, is one-tenth of the amount of Vitamin 'D' which will change the faecal pH of rats from an average value of 7.3 to an average value of 6.7 in not more than seven days.

For the purpose of comparison, the second unit may be regarded as approximately equal to five Coward units.

Antirachitic value of Cod Liver Oil. The children of the Island of Lewis, in spite of bad domestic conditions, are relatively rickets-free. The explanation is the large use of cod livers—a first-rate antirachitic, and the plentiful use of oatmeal, eggs and fish. Remarkable immunity to rickets of Jews as against Gentiles. Dietary of the former includes much fatty foods—oil, eggs and milk.—E. Mellanby, L. i./20,856. See also Roy. Soc. of Med., Discussion, *ibid* 604.

The thyroid gland was examined of dogs fed on diet containing various fats. When fed on butter, cotton-seed or linseed oil the thyroid was invariably large, and resembled that of Graves's disease, whereas on a diet of Cod Liver Oil it was small and histologically normal.—E. Mellanby, B.M.J. i./21,779.

Vitamin 'D' has powerful inhibitory effect on the **formation of caries** in children.—May Mellanby and C. L. Pattison, B.M.J. ii./28,1082. Criticisms of theory.—H. Campbell, *ibid*, 1155 and J. S. Wallace, *ibid*, 1156.

Irradiated Cholesterol (a 3% solution in Linseed Oil) cured rickets after Cod Liver Oil had failed. **Dose.**—1 to 2 drachms three times daily. Irradiated Cholesterol loses its antirachitic power when kept. Prolonged exposure to Ultra-Violet Rays should be avoided, as this renders it inactive again. Cholesterol is more soluble in Colza Oil, and also dissolves easily in warm Liquid Paraffin.—L. G. Parsons, B.M.J. i./26,520.

Actinotherapy in treatment of rickets rapidly becoming a thing of the past. Irradiated Ergosterol more effective than Cod Liver Oil or Ultra-Violet Rays.—R. Aidin, L. i./28,229.

Antirachitic properties can be imported by Ultra-Violet irradiation on Phytosterol, Cholesterol, vegetable oils, and on etiolated and green wheat or lettuce leaves. In the activated oils **the active substance** was found to be **in the unsaponifiable fraction**. Irradiation does not activate Chlorophyll, hæmoglobin, red-blood corpuscles, cream, glycerol or phosphatides of egg yolk.—A. F. Hess, M. Weinstock and F. D. Helman, JI. Biol. Chem., '25,297,335; J.C.S. Ai./25,750.

Fresh spinach leaves contain a large quantity of Vitamin 'A,' but no detectable Vitamin 'D,' except in mid-summer when they contain a small quantity, but when irradiated for 30 minutes at a distance of 36 cm. from a quartz-mercury vapour lamp just prior to consumption they become powerfully antirachitic.—B.M.J.E. i./26,66.

Query as to length of time Vitamin 'D' keeps in margarine.—N. Evers, P.J. ii./28,579.

Rickets will soon become a disease of great interest to the historian but will present no terrors of ill-health for the patient or cause for anxiety of the doctor.—L. G. Parsons, L. ii./28,489.

Patent rights granted to the Alumni of Wisconsin University for use of ultra-violet light for improving foodstuffs—rights used for the furtherance of the University. Biological inventions subserving medical treatment should not be patentable (Brit. Sci. Guild).—F. H. Carr, P.J. ii./28,579.

Vitamin 'D' should be tested for in addition to 'A' in Cod Liver Oil in U.S. Prof. Poulsson's method, using X-Ray photos of the degree of rickets before and after 6 days, and the gain in weight, is used. Norwegian Oil thus has 450—500 'A' units and 200—250 'D' units per Gm.

It has been found that Cod Liver Oil given during pregnancy prevents recurrent abortion.

The now well-known Sterol-ergosterol, as precursor of 'D,' is described. Activated Ergosterol is 100,000 times as active as Cod Liver Oil. It is by far the most potent antirachitic substance known (Hess and Lewis, JI. A.M.A., Sept. 15, '28), and it is specific. The percentage of Calcium and inorganic Phosphorus in the blood enables accurate estimation.—J. W. England, JI. Am. Ph. Assn., Feb. '29.

III—Effects Possible.

Irradiated Ergosterol given by the mouth in very large doses causes the formation of **urinary calculi**. It is suggested that this is dependent on an increased absorption of Calcium and Phosphate from the gut and their excretion by the kidneys.—W. E. Dixon and J. C. Hoyle, B.M.J. ii./28,833.

Toxic effects from Irradiated Ergosterol only produced when given in enormous excess, and poisoning is not a probable danger in clinical practice.—B.M.J. ii./28,856.

Daily doses of 2.5—5.0 mgr. Irradiated Ergosterol remarkably effective in rickets, but there is evidence of hypercalcæmia even with these doses, and the dosage for free use should be carefully considered.—L. ii./28,827.

The quantity of Vitamin 'D' which proves toxic to a rat is some 100,000 times an adequate 'physiological dose.' There should be little practical danger to humans of ill-effects from excessive Vitamin intake.—L. J. Harris and T. Moore (Nutritional Lab., Med. Res. Council), L. ii./28,893.

VITAMIN "E"

The most active preparation of Vitamin 'E' is made by fractionation of the unsaponifiable matter of **Wheat Germ Oil**. A sterol-free fraction distilling at 225°—230° C. at 0.01 mm. pressure contains the whole activity of the oil. A dose of 5 mgr. fed to otherwise sterile female rats upon the day of mating suffices to ensure normal gestation. **Vegetable foods**, especially **Lettuce and Wheat Germ**, are the most potent sources of this Vitamin. It is not destroyed during cooking plant or animal tissues, but the latter are relatively poor sources of it. It is not easily oxidised.—H. M. Evans, G. O. Burr and T. L. Althusen, "The Memoirs of the University of California," Vol. 8—a concise summary was published in 'Nature,' July 28, 1928.

It is growth-promoting, as are all the Vitamins.—K. H. Coward, P.J. ii./28, 572.

BREAD AND FLOUR CONTROL.

Flour Bleaching and Improvers.

Civilised man living a normal life, derives a large portion of his carbohydrate intake from cereal foods. The Anglo-Saxon, the Latin and the Teutonic races have chosen wheat flour or meal as their main cereal food. A portion of the Teuton races and of the Eastern peoples use a considerable quantity of rye flour.

Dr. J. M. Hamill's Food Report No. 14, 1911, to the L.G.B., enumerated milling products in common use as follows:—

'Wholemeal' or 'Graham Flour' (actually whole grain flour).

'Entire Wheat Flour' or "Fine Meal"—a product obtained by removing a portion of the bran and grinding the rest of the grain. (This includes so-called "Standard" Flour).

'Households'—The commercially lower grade of flour obtained from roller mills—it is darkish in color.

'Patent Grade.'—Commercially the higher grade flour produced by roller mills. It is a better color than any other flour produced in the mill.

'Straight run' or 'straight grade'—intermediate in appearance and quality between households and patent grades.

Special flours, prepared from any of the above usually with the object of improving nutritive qualities.

The following **special** distinctions have recently been applied to **stone ground flour**:

(1) "Stone-milled" flour refers to any flour produced by stone-grinding.

(2) Wholemeal flour contains all the constituents of the original grain, including bran and germ.

(3) Millstone flour contains all the constituents of the grain, *except* the bran. It includes 87 to 90% of the germ. It keeps well under proper conditions.—C. E. Shelly, B.M.J. i./24, 1883; ii./24, 720.

In regard to the question of the best type of flour and bread made from it, Dr. Hamill, in the same report, says:—

The great practical difficulty in endeavouring to define any one variety of flour in terms of protein content, mineral content, or other criteria, is that such a definition to be effective would require preliminary standardisation of wheat which is impracticable in view of the fact that wheat supplies vary from different parts of the world. It is evident that, unless we live wholly on bread, which is not desirable, the differences between one bread and another do not matter much.

With regard to choice of bread for children, however (though here also a varied diet is insisted on) it is stated—"For those children who live largely on bread—there appears to be advantage in bread from flour of the '*entire*,' wheat class or from wholemeal in which the bran is very finely ground. In these the presence of the so-called *offal*, including the germ, secures a somewhat larger quantity of mineral matter and of suitably combined Phosphorus or other substances as yet unknown, which has been proved to be of importance.

The above view is illustrated and supported by taking one factor alone—the Albuminoid content. The albuminoids in a variety of wheats—Argentine, Australian, English, Canadian, Indian, etc.—may range from 8 to 16% of the grain.

Grain arrives in this country from various parts of the world at divers times of the year, according to the respective local seasons, and the miller's labours are taxed to blend these wheats of varying qualities to produce a grist which when milled will provide a flour suited to modern baking methods.

Wholemeal v. White Bread

The controversy as to the respective merits of wholemeal and white bread has produced a constant stream of literature for a generation and the battle of opinions is still with us.

The Standard Bread agitation started in 1911.

Standardisation of flour, as originally understood, is impossible,

but its control is *as important as*, if not *more important than*, the standardisation of Drugs, and the quality of Flour (and other foodstuffs) should be kept at the *highest possible level*.

The author (W. H. M.) communicated a paper on the so-called "Standard Bread" to the "Chemist and Druggist" (C.D. i./II, Index Fo. 321), which may be consulted, as also the 17th edition of this volume.

"Standard" bread was defined as bread made from unadulterated wheat flour containing at least 80% of the whole wheat including the germ and semolina.

A glance at the sectional diagram of a grain of wheat, *e.g.*, as shown in the Food Report referred to, or in Jago's "Science and Art of Breadmaking," shows the situation of the "germ" (a small portion of the entire grain) in the grain and enables one to understand the reason why it is in great measure winnowed away by the roller process of milling. The husk or outer envelope yields the bran, and consists roughly of cellulose and salts; the endosperm yields the starch; the germ is rich in protein and fat.

In the roller process of milling, as now generally conducted, about 72% of the cleaned wheat is obtained as white flour. This contains more or less of the *aleurone* layer, which is rich in protein and phosphorus compounds, and most of the "starch" cells of the original kernel.

Each cell contains hundreds of starch granules embedded in the protoplasmic material composed of protein matter, in this case gliadin and glutenin. It should be clear that even the whitest and most starchy part contains a significant amount of protein. Higher grades of flour are characterised by a lighter colour, more elastic gluten, better granulation, and a smaller number of debris particles. Low grade flours contain a somewhat higher percentage of protein, but are not so valuable for breadmaking, because the gluten is less elastic.

Spring wheat, grown mainly in the North-Western States and in Canada, is usually harder and slightly richer in protein than the winter wheat which is somewhat more starchy. In general, a rather hard wheat of more than average protein content is preferred for the manufacture of bread flour, but the wheats with most protein do not necessarily make the best flour.—Food Products (1924), H. C. Sherman.

The word 'Semolina' is given to varied products according to the fancy of the miller. The dictionary application of the name is "coarsely ground and carefully purified milling products, especially hard wheat used for macaroni and in cookery." Others apply it simply to a 'physical condition' of flour. Others, again, definitely hold that the semolina obtainable commercially is the hardest portion of the endosperm of the wheat grain and is obtained in a granular form by adjusting the rollers sufficiently far apart, so as not to crush the granules. The following definition is given in a work of reference.

SEMOLINA. (F. Semoule). A wheat meal prepared from the large grains of the hard wheats of Southern Europe by a special process of milling, which produces a very white coarse flour, rich in gluten, rendering semolina a valuable flesh-forming food.

Semolina appears to us a product of some value in milling, and not merely 'a physical condition of flour.'

The germ differs considerably in composition from other parts of the grain. We have placed side by side (from W. Jago—transposed from his figures into percentages) the amounts of certain constituents of a (a) wheat mixture, (b) one of the semolina products—that coming from the second and third "breaks," (c) "Flattened Germ" from the same mixture and (d) Bran:

	Wheat.	Semolina.	Flattened Germ.	Finished Bran,
Moisture ..	38.171	43.041	14.822	22.598
Soluble extract ..	16.403	13.577	43.940	17.567
Soluble protein..	4.361	3.191	15.652	2.259
Crude gluten (dry)	19.093	19.416	—	—
Ash ..	4.835	3.394	5.501	12.742
Phosphoric Acid	2.465	0.747	3.207	7.322
Fat ..	4.993	4.311	11.982	3.068
Cellulose ..	9.671	12.627	4.776	34.4

Note the figures for "Soluble Extract," Protein, "Ash," Phosphoric Acid and Fat in the Germ in comparison with Wheat, also the figures for Ash and Phosphoric Acid of Bran compared with those in wheat.

In a Memorial to the then Min. of Health on the Advisability of introducing measures to protect Meal, Flour and Bread from Deterioration and Adulteration, presented in the House of Commons, Dec., 1919, S. Rideal pointed out that the millers get **good prices for offals** for cattlefood, hence **the wheat is not used to best advantage** of the human consumer. Sir F. Fox at the same Meeting said that the process for removal of the germ (and the color) was discovered by Hungarians, who took the idea to America and from there it came to us. Hence the very white flour.

Suggestion to raise the 'standard' to even 90%—this is quite palatable.—D. Noel Paton, B.M.J. i./25,170.

Although the difference in protein between roller-milled flour and stone-ground flour is not great, it is the **quality not the quantity of protein** that matters, and the proteins of the germ are particularly suited for promotion of growth. In the case of children who have abundant mixed diet this special protein is obtained from other sources, but where the diet is mainly composed of bread the difference might be of considerable importance.—R. Hutchison, B.M.J. ii./24,720.

Mineral constituents in the ash of wheat and other cereals:—Lime, it has been stated, ranges from 1 to 10%; Magnesium Oxide gives an average of 12.11%; Silica rarely reaches 5%, being usually less than 2%, P_2O_5 constitutes an average of 49 to 50%. Iron as Fe_2O_3 averages 1.1%.

Figures giving flour analyses vary greatly (cf. Atwater and Benedict, Hutchison, Tankard, etc.).

Iodine in wheat products. Bran contains 3.8, germ 3.0, and whole-meal 2.5 parts per million. **White flour contains less than 1 in 5,000,000.**—B.M.J. i./25,764.

White flour and bread are robbed by the miller of Iodine, along with valuable salts and Vitamin B.—Review of Swale Vincent's book on Internal Secretions and the Ductless Glands.—B.M.J. i./25,369.

Copper occurred in bread from the Acetic and Carbonic acid of fermentation attacking bronze parts of machinery.—T. H. Gardner, B.M.J. ii./25,798,

Nature, of May 4, 1911, had a good article on the position on this and allied matters:—

The outer coats of the grain yield bran, fine pollards, sharps, and middlings, the germ is removed as offal, while ordinary flour is derived almost solely from the endosperm. The flour itself is divided into a larger portion, "bakers" or "households," and a smaller, very white and poor in protein, known as "patents," from which genuine Vienna bread and the best class of fancy breads and pastries are made. The semolina, derived from the central parts of hard wheat, and rich in gluten, is also lacking in white flour.

It will thus be seen that ordinary white flour and white bread made therefrom contain little or none of the bran, germ, and semolina, and valuable food constituents—mineral matter and protein of the bran and semolina, and fat and protein of the germ—are lost. Wholemeal bread is therefore richer in the nutritive constituents and has more flavour, but is darker in colour than white bread, owing partly to the inclusion of the bran and partly to an interaction by which dextrin and sugar are formed which undergo darkening in the oven. Wholemeal bread is, however, apt to be irritating on account of the cellulose and silica of the outer coat, but by removal of the outer layers of the husk the irritant material may be excluded, and the valuable mineral, protein, and fatty constituents of the inner branny coat, semolina, and germ, retained. Such a flour constitutes the "80 per cent. flour" employed in making the so-called "standard" bread. The term "80 per cent. flour" means that a wheat, a bushel of which weighs 64 lb., yields 80 per cent. flour. In the old method of milling, the wheat is ground between stones, the flour being separated by sifting, and in this way some of the "offal" is retained: hence the term "stone-ground."

There is doubtless some difference of opinion as to the relative values of ordinary and "standard" flour, and the bread made therefrom. The roller mills cleanse the wheat in a very efficient manner. Analysis, except *re* salts, shows little difference; "standard" bread may even be slightly poorer than ordinary bread in protein, owing to the greater percentage of moisture.

Rats were fed for three weeks, some on standard bread and some on white bread, and for a second three weeks on white and "standard" flour. It was found that rats can thrive and be reproductive on wholemeal and water. A diet of white flour and water is more harmful to young rats than old. Germ and bran are needed above all for growth.—Leonard Hill and M. Flack.

With regard to the **Phosphorus** in wheat bran,—this was first thought to be inorganic—then to be connected with the nuclein or salts of Nucleic Acid—but researches show that only 33% of the Phosphorus could be accounted for in this way, and that the chief Phosphorus compound is a Magnesium-Calcium-Potassium Salt of a Phospho-organic Acid,—probably identical with Anhydro-oxy-methylene-diphosphoric Acid,—an acid which is widely distributed in the vegetable kingdom.—B.M.J. ii./11,861, 1137.

The higher animals are apparently not endowed with power of preparing their own organic phosphorus compounds from inorganic phosphorus, nor indeed, are they probably able to form such compounds of one group from those of another. These bodies are of far-reaching importance to the bioplasm.

A healthy man accustomed to a full mixed diet requires for maintenance of phosphorus equilibrium about 1.5 Gm. of phosphorus, or nearly 3.5 Gm. of Phosphoric Acid *per diem*; the organic combination seems to be the best. The calcium requirement is equivalent to about 0.7 Gm. of Calcium Oxide *per diem*.—Na., Dec. 1, 1910, p. 148.

Amino-Acids (Asparagin, Leucin and Trypsin) are no doubt of importance. According to Tibbles, it is to the greater amount of these in the germ and cereal in that one may look for the different effects obtained by feeding with flours of various grades.—B.M.J. ii./11,1137.

Feeding experiments show clearly that **Histidine** is one of the growing list of known indispensable amino-acids, and there is reason to believe that Histidine is essential in nutrition because it is required for nuclear synthesis in which purins play an outstanding part.—Jl.A.M.A. ii./25,830.

L. Hill and M. Flack stated: "**Wheat germ alone added to white flour** makes this an adequate food on which animals can live healthily. This proves that the lack of Cellulose has nothing to do with the insufficiency of white flour, and that whatever the active principle may be, it

is present *no less in germ than in bran and sharps*. In fact, rats did better on white flour plus germ than on white flour plus sharps, bran, and a trace of germ."

Vitamin 'B' Content of White Bread and Flour—Rat experiments showed that mothers fed with extract made from wholemeal flour did better than those fed on extract from white flour, *i.e.*, there is more Vitamin 'B' in wholemeal than in white flour. The author concludes that white bread contains sufficient Vitamin 'B' to supply the needs of a rat both for growth and reproduction. White flour contains a little Vitamin 'B,' but the main source is the yeast.—Gladys A. Hartwell, *Biochem. Jl.*, Vol. XVIII., No. 1, 1924.

Whilst the addition of yeast has no material affect on its 'B' content the addition of Wheat Germ produces a bread rich in Vitamin 'B' and yet distinct from wholemeal bread which contains bran—an indigestible substance.—W. Cramer and J. C. Mottram. *L. ii./27,1090*, see also *ibid* 1153.

Bulk for bulk, white bread has more calories available for nutrition than brown bread. Vitamin 'B' is present in the yeast introduced into the white bread and if the effect of the "roughage" is to produce instead of a formed stool one of more fluid consistency it is doubtful whether it confers any known benefit on a healthy person.—Sir T. Horder, *L. ii./27,103*; see also *ibid* 201.

Yeast may be dispensed with, and actually much bread on the market to-day has been aerated by incorporating already-formed Carbon Dioxide with the dough. If Persulphate of Potash be used as an improver, Ammonium Persulphate may be formed by the gluten, and this, acting as a reducing agent, is likely to destroy any Vitamin introduced by the yeast.—J. Oliver, *L. ii./27,254*. ('Improvers' are dealt with later).

Unable to keep rats alive longer than 5 weeks on a 'B'-deficient diet, whereas the addition of Wheat Germ 2% enabled them to live normally.—M. J. Rowlands, *L. ii./27,305*.

It has been shown that the highest proportion of Yeast (fresh) normally employed in bread-making will not supply white bread with more than 1/7th the amount of Vitamin 'B' found in good wholemeal bread, and it has been proposed to solve the problem by replacing white by wholemeal bread. Such a replacement, however, would create serious milling difficulties and would involve extensive alteration, or even scrapping, of much expensive milling plant, with a consequent rise in the cost of the bread. A practical alternative is the **addition of dried yeast** to ordinary white flour. **Dried yeast** is several times **more potent** in Vitamin 'B' content than the fresh yeast employed in bread-making, and if used in a proportion of 2 to 4% would yield a palatable bread containing as much Vitamin 'B' as the finest wholemeal product.—S. G. Willimott and F. Wokes, *L. ii./28,673*.

Robert Saundby communicated a paper on food and feeding. (*B.M.J. i./11,1218*). The following is an abstract:

The public were asked to adopt the view that 'white bread' is deficient in nitrogen and inferior to bread made from flour containing the whole of the constituents of the grain. **Wholemeal or Graham Flour**.—No objection can be made against white bread so long as this is not due to chemical bleaching. (For the subject of bleaching *vide* later.) It must contain weight for weight as good proportions of protein, carbohydrate, mineral matter and fat as the 'standard' article. The **moisture** in bread varies from 30 to 40%. In Columbia, U.S.A., the proportion is regulated by law to 31%, but here there is *no legal limit*. Excess of gluten produces a loaf that retains moisture. Beri Beri (*vide* also *Vol. I.*, pp. 593, 877 and *Vol. II.*, *postea*) is associated with eating completely shelled rice. *Vitamins are removed in the 'polishings' which are of great importance, and similar conclusions may be drawn re white flour*. **DENTAL CARIES** has been thought to be due to the softness of white bread, but

'standard' bread is just as soft, and the natives of South Africa, India and Japan subsist on soft starchy foods and have good teeth. Caries is more likely to be due to excessive consumption of sugar, which rose from 30 lbs. per head in 1864 to 89 lbs. in 1910.

The therapeutic value of **FASTING** is carefully considered in this paper. Disappearance of or amelioration of many chronic ailments after fast has been proved in Rome; prison diet has been shown to have similar effect. Fasting in diabetes is of value.

Increase in acidity of Bread during Mastication.

Hill and Flack conducted some experiments on this subject. They did not find any marked difference between the acidity produced on masticating white and wholemeal breads (it has been said that decay of teeth is due to acid production from white bread).

Flour of the 'Standard' type must contain more protein, fat and ash, than fine white flour made from the corresponding wheat or mixture of wheats.—W. A. Bond, L. i./11, 1669.

The introduction of the steel 'roller flour mills' into this country from America inflicted a vital injury on our national well-being, for **the roller-mill extracts from the wheaten berry the "germ" which contains the essential nourishing matter of the grain, the residual flour consequently consisting of little more than mere starch. It lacks some of the proteins, fats, vitamins and mineral constituents present in the original grain, providing an emasculated substitute, not only inefficient but directly harmful.** The future of a nation thus deprived of its essential nourishment is gloomy in the extreme. The Americans themselves regret the use of the steel roller mills. Legislative support of the old stone-milled flour needed. —C. E. Shelly, B.M.J. i./24, 798.

The above information should be considered with the latest theories on Vitamins, for details of which see Vol. I., p. 592, and the additional chapter on the subject in this volume.

Comparative compositions of white and wholemeal bread are :

	Carbohydrate	Fat	Protein	Ash	Water
White	51.5	1.0	6.5	1.0	40
Wholemeal ..	46.3	1.2	6.3	1.2	45

Wholemeal bread thought to provide valuable proteins (with Vitamin 'B'), salts, and "roughage."—C.D., Jan. 24/25, 139.

National Mark Flour is in **Three Grades.**—

ALL-ENGLISH (Plain).—A general purpose flour, but mainly for biscuit-making.

ALL-ENGLISH (Self-raising).—Household flour for pastries, puddings, etc.

ALL-ENGLISH (Yeoman).—A bread-making flour made of Yeoman wheat, the variety created at Cambridge by Sir Rowland Biffen to produce a loaf equal to that made of best Manitoban wheats.

★ **Vita (T.M.478,917) Wheat** is thoroughly cooked. The bran is subjected to a preliminary cooking before the final baking.—B.M.J. ii./27, 21.

★ **Energen (T.M.337,793) Bread**, according to the makers, is prepared without Yeast, drugs or chemicals, and contains but one-fifth of the moisture usually present. Over 40% of the wholemeal bread consists of whole wheat berry.

Bleaching of Flour.

Bread is sold legally by weight, and too often the baker slack-bakes his loaf and leaves as much water in it as possible (it should not exceed 15%—Kenwood), in consequence it is less digestible,

more dough-like and less nourishing. Bread ought to be sold, as pointed out by the B.M.J. a few years ago, as containing a given weight of the food principles found in wheat, *i.e.*, not less than so much protein, so much carbohydrate, and containing all the principles which suffice to support the nutrition of pigeons when they are fed on bread and water.

The bleaching of flour by chemical process is unnecessary.

The United States Government in 1910 took action against certain flour millers in regard to 625 sacks of flour which were alleged to be adulterated, and after trial the Government authorities proved their case and the flour was condemned. It had been bleached by the 'Alsop' process. "The essential apparatus in this process is a small chamber with two electrodes. One of these electrodes is stationary; the other is raised up and down by a suitable crank motion, so as to approach the first. These electrodes are charged with a heavy current of electricity. When the points of the electrodes touch, the current flows just for a second, and when they are pulled apart a flaming discharge takes place between the two. This discharge is of a high temperature—so much higher than the ordinary temperature of combustion that it causes the nitrogen and oxygen in the air to combine, actually to burn, and the result is **nitrogen peroxide**. While the electrodes are in operation, a current of air sweeps out the nitrogen peroxide, and a further supply of air is drawn in. After being swept along, the nitrogen peroxide is carried by a tube to a box, which is provided with a rotating apparatus. To this box, called an agitator, comes the finished flour from the mill, and is made to fall down through the nitrogen peroxide and air. During this passage the bleaching is effected."—From a bulletin by the U.S. Dept. of Agriculture.

The result is that the flour contains an appreciable amount of **Nitrites**. The physiological effect of this flour, when made into bread, has been described as 'disastrous' to many.

Bleached Flour is prohibited by law from sale in the U.S.A., but it is exported to this country for sale.

It has been claimed that bleaching is to the benefit of both the miller and the consumer, but our view is that it assists the former and is bad for the latter.

In a Local Government Board Report (Food Report No. 12, 1911) Drs. J. M. Hamill and G. W. Monier-Williams dealing with the action of **Nitrogen Peroxide** (N_2O_4) indicate that the color of the bleached flour may change again, *i.e.*, become yellow or still more bleached according to circumstances. The quantity of Nitrous Acid or Nitrites formed is proportional to the N_2O_4 used. The N_2O_4 is present in the flour as **Nitric and Nitrous Acids or Nitrates and Nitrites**. In highly bleached flour (1 kilo with 300 Cc. of N_2O_4) an increase in the amounts of soluble Proteins and soluble Carbohydrates takes place. The amount of soluble Nitrogen is doubled (due entirely to the solubility of Gliadin in HNO_3 of certain strengths). About 6 to 7% of the Nitrogen

introduced as N_2O_4 —is absorbed by the fat of the flour—it undergoes change like an oxidised oil. The rate of digestion was greatly retarded if the starch had been previously treated with N_2O_4 . *Bleaching exercised an inhibitory effect on the salivary digestion of flour.*

As an average, we believe that in the neighbourhood of 3 to 50 Cc. of the Oxides of Nitrogen per kilo of flour is employed.

In commenting on the above report, the "Lancet" (L. i./11,1024) stated that steps taken by other countries, *e.g.*, Australia, U.S.A. and Switzerland, to banish by statute the practice of bleaching, should be a useful object lesson to the legislators of this country. The process cannot be viewed as free from risk to the consumer—especially in regard to the inhibitory effect on digestive processes and enzymes. (*Halliburton has stated that the bleaching of flour by Nitrogen Peroxide renders the gluten indigestible.*)

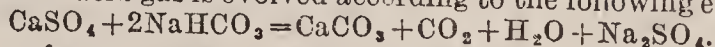
"The Nature of the Colouring-matter of Flour and its Relation to Processes of Natural and Artificial Bleaching." G. W. Monier-Williams in a L.G.B. Report showed that the colouring-matter is either carotene or a substance allied to it. The colour of this body is discharged by oxygen or by nitrogen peroxide. On exposure to the air it is bleached by absorption of oxygen, no oxides of nitrogen being absorbed, and the natural ageing of flour may be a similar process, while in the bleaching of flour by nitrogen peroxide substances are produced which are not produced during the natural ageing of flour. Unbleached flour contains some nitrite reacting substance, but this is equivalent to not more than 1.5 parts of sodium nitrite per million; the effect of excessive bleaching on the baking qualities of flour is dealt with.

It is stated (J.C.S.I., Jan., 1912, p. 40) that Nitrites *do not interfere with the action of diastase on starch*, also that *pancreatic digestion is not inhibited by relatively large quantities of Nitrites*. Further, that direct experiments with the compound of the colouring matter of the flour with oxides of nitrogen showed that this is not poisonous nor does it have any perceptible action on the blood.

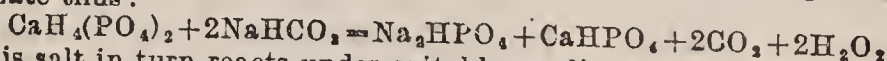
Calcium Sulphate in Baking Powder and Self-raising Flour.

Baking Powders, according to a L.G.B. Report on 'the presence of Calcium Sulphate in Baking Powder and Self-raising flour' (Food Report No. 13, 1911, by Dr. Hamill), in use may be classed into two groups (1)—this being far the larger—tartaric powders in which the acidic constituent is tartaric acid, cream of tartar, or a mixture of these, and (2) the phosphate powders, the acidic constituent of which is acid calcium phosphate, together with sodium bicarbonate in all cases. Ammonium carbonate is extensively used *per os* as a necessary ingredient in the baking of sponge cakes and other light bread products. Alum is not now employed, although it is capable of acting as an acidic constituent, and was formerly much used. In an addendum by C. H. Cribb, regarding the use of phosphate baking powders and the alleged utility of calcium sulphate in them, it is stated:

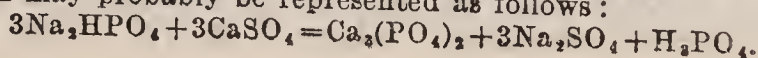
When calcium sulphate is mixed with sodium bicarbonate in the presence of water, carbonic acid gas is evolved according to the following equation:—



The evolution of gas commences immediately, but is very slow, so that at the end of $\frac{1}{2}$ an hour 59 per cent. and after one hour 79 per cent. of the theoretical quantity was found to have been liberated, and even after three hours the reaction was not complete. When acid calcium phosphate acts upon sodium bicarbonate one of the products of the reaction is hydrogen disodium phosphate thus:



and this salt in turn reacts under suitable conditions with calcium sulphate, giving rise to phosphoric acid, which in turn can liberate a fresh quantity of carbon dioxide from any carbonate which may be present. The first part of the reaction may probably be represented as follows:



In actual baking experiments with a baking-powder containing calcium sulphate, 75 per cent. of the calcium sulphate was recovered unchanged from the finished loaf. Other experiments would seem to indicate that the calcium sulphate which has disappeared as such in the loaf is again re-formed by the agency of the acid in the gastric juice when the bread is eaten.

Calcium Sulphate occurs in commercial acid calcium phosphates to the extent of 2 or 3 per cent. up to 50 per cent. The proportion varies according to the method of preparing the calcium phosphate.

It is generally made from bone ash by means of phosphoric and sulphuric acid. When commercial phosphoric acid only is added to the bone ash, a product can be obtained containing as little as 2 per cent. or as much as 9 per cent. of calcium sulphate. When sulphuric acid alone is used, the product **may contain as much as 50 per cent. of calcium sulphate**; mixtures of these acids give values intermediate between the extremes mentioned. Calcium sulphate is sometimes deliberately added as a diluent. To keep the acid phosphate and sodium bicarbonate from too intimate contact, a neutral non-hygroscopic powder, known as 'filling,' is added, such as corn flour or more usually rice flour. The filling may be 50% or more of the baking powder.

The following recipes are given in the report:

Calcium Acid Phosphate	50	..	37	..	2	..	77
Sodium Bicarbonate	25	..	23	..	1	..	41
Maize Starch, rice-flour or ground									
rice	25	..	40	..	3	to 10	50 to 100

From $\frac{1}{2}$ oz. to 1 oz. of the powder is used for each pound of flour, hence if the calcium acid phosphate of the first powder contained 50% of calcium sulphate $\frac{1}{2}$ oz. of the powder would contribute **over 50 grains of calcium sulphate to the flour**. The same remarks apply in regard to the calcium sulphate introduced with the phosphate, 70 grains per lb. being contained in the above flour if the first ingredient is 50 per cent. phosphate. The phosphate baking powders do not keep well and are not found in retail trade. Bakers mix the ingredients when required. **Self-raising flours** are made thus:

Calcium acid phosphate	6 lb.
Sodium bicarbonate	3 lb.
Flour	280 lb.

Dr. Hamill made the following recommendations (*inter alia*):

(a) *Manufacturers of acid phosphates* should not prepare even their cheapest qualities of acid phosphate, for sale as food ingredient, in such a way that they contain more than 10 per cent. of calcium sulphate.

(b) *Bakers, self-raising flour makers*, and others using acid phosphate in the preparation of food, should limit themselves to acid phosphate of high commercial quality—calcium sulphate not to exceed 10 per cent.—L.G.B. Report and Editorial comment C.D. i./11, Index Fo. 545.

(We believe that users of the acid phosphate in question now stipulate considerably less than 10%.)

Alum in Baking Powders.

Experiments on mice show that bread containing Aluminium Phosphate causes necrosis of the stomach epithelium and the tops of certain intestinal villi; in dogs lesions are caused in the descending colon and the sigmoid flexure. Aluminium appears to have a specific action on the ovary—the productivity of female mice is diminished if fed on Aluminous diet and the offspring succumb more easily to infantile disease. Experiments on human beings showed that baking powder containing Alum, when taken alone, caused diarrhoea and painful indigestion.—L. ii./28,456.

Improvers.

Sodium Chloride has long been used, the usual amount being $3\frac{1}{2}$ lbs. per sack of flour.

Gelatinised Potato, or, as it is called, "Fruit," has been used to assist the yeast plant in its function of vesiculating and maturing the dough with the least trouble to the baker.

Sour Flour also materially improves baking qualities, when added in the amount of 5 lbs. to 275 of fresh-milled flour.

Acid Salts (Persulphates and Acid Phosphates). The yeast plant develops best in a medium possessing definite acidity, and there must be available in the dough a supply of nitrogenous food and of the phosphatic sugar complex. The addition of acid enables the British miller to compete with overseas competitors. Previously, it is stated, overseas flour was improved in transit, both in colour and acidity, making it more desirable from the user's point of view for baking without yeast.

With regard to flour for yeast panification, here also acidification is desirable. It was found that a flour, for example—to give an extreme case,—containing 12·71% albuminoids and a wet gluten figure of 39·4, gave a loaf badly aerated and with a crumb like indiarubber. The addition of $\frac{1}{2}$ ounce of Ammonium Persulphate per 280 lbs. of flour changed the character of the flour and gave a good loaf. On the other hand, a flour with 8·2% albuminoids—and correspondingly more carbohydrate—and wet gluten 24·67 gave an excellent loaf.

Acid Ammonium Phosphate to the extent of, say, 4 ounces per sack, it is claimed, will provide a nitrogenous food for the yeast and will provide the necessary acidity. It may be used in conjunction with Acid Calcium Phosphate.

Persulphates are stated to act like Acid Ammonium Phosphate as stimulants in a dough made of flour, yeast, salt and water.

Chlorine.—The use of this is said to be beneficial, in rendering flour amenable to maturation by yeast.

Suggested maximum quantities are:—

Acid Calcium Phosphate	..	0·3 %	= 13½ oz. to 280 lbs.
Acid Ammonium Phosphate	..	0·2 %	= 9 " " "
Persulphates	..	0·04 %	= 1·8 " " "
Chlorine	..	0·07 %	= 3 " " "
Nitrogen Peroxide	..	8 parts	of nitrites per million.

A mixture in about equal proportions of Acid Potassium and Magnesium Phosphates and flour is said to be an effective "improver."—Public Health Lab. Work, Kenwood.

Treatment of flour is also carried out in Germany, Holland and other countries. In favour of Persulphates.—W. Jago, L. ii./26,1038.

Persulphates and other chemicals are foreign additions to flour, and constitute when added to flour substances which render this food *not of the nature of flour*.—A. R. Tankard, L. ii./26,1243. *We agree.*

"BAKER'S ECZEMA" due to use of flour containing Potassium Persulphate to the extent of 6·3 parts per 100,000.—A. R. Tankard, L. ii./23,279.

There should be no difficulty in tracing the use of improvers, the commonest being Potassium Persulphate.—J. T. A. Walker, L. i./25,1163; *See also* 1273.

'BAKER'S ITCH.' Immunity of French and American bakers to this is attributed to the fact that the use of 'improvers' is illegal in those countries. One of the commonest 'improvers' to which the complaint may be traced is Potassium Persulphate, which decomposes on addition of water with liberation of Oxygen and formation of Potassium Acid Sulphate, the reaction being expressed thus: $2K_2S_2O_8 + 2H_2O = 4KHSO_4 + O_2$. Baker's itch was unknown in this country before introduction of 'improvers.'—J. T. Ainslie Walker, L. i./25,1163.

IMPROVERS AND DERMATITIS. Dr. Parsons on behalf of the Ministry of Health made investigations on the subject in the early part of 1922. Among

the conclusions were that probably 50% of cases could not be true bakers' itch acquired as result of baking. During the war and the period of demobilisation the term was widely used as an euphemism for scabies and heterogeneous skin lesions. Trades unionism found to be correlated with the subject. Medical opinion was that no increased prevalence of the true complaint was found. Contact with *Sugars* and not foreign flour or bleaching processes accounts for a large proportion. Machinery avoids mechanical irritation of the dough. A small % of cases found in which after years of immunity a baker may become sensitised to flour protein. 2 cases were found.—National Bakers' Assocn. Review, Nov. 9, 1923.

Detection of Potato Starch in Bread.—Moisten a small piece of bread crumb, crush to a paste on a slide under a cover glass. Starch grains from raw potatoes are recognised by their ovoid, highly refractive, three or four cornered, smooth granules with deep furrows running lengthwise. If boiled potatoes have been used, granules are absent and the cells usually round and elliptical.—P.J. ii. 15,549.

Some forms of Food Adulteration. Governments of the last half century have been content to allow the subject to be dealt with in a perfunctory manner. Food adulteration is actually a science. Bakers have no knowledge of the chemical character of the improvers added by the millers. Yeast adds Vitamin 'B,' but when leavening is done by CO_2 no Vitamin is added. Improvers may also destroy it if Yeast is used. Chlorine is the favourite bleaching agent to-day.—James Oliver, M.P.C., Nov. 7/28,384.

Heat Treatment of Flour. Weak flours have their protein in an insufficient degree of aggregation. By heating in an enclosed space to 180°F . for 10 to 12 hours they acquire 'improving' properties, and are useful to add to ordinary flour to the extent of 0.7%.—D. W. Kent-Jones, 'Modern Cereal Chemistry.' We tried the experiment ourselves. Beyond the baking effect, there was nothing remarkable in the product. Probably a higher temperature is needed than that stated.

Analysis of Flours.

A few years ago—in 1925 (see Edn. XVIII., Vol. II., p. 112) we found the ash-percentage in flours bought in various parts of London to be within normal limits—approx. 0.3 to 0.5%. It is generally understood that an ash of 1% would indicate mineral adulteration or low-grade flour.

In the case of Self-raising Flour, several samples showed about 2% of inorganic residue on ignition.

Detection of Bleaching of Flour.

This can be effected by the production of a red colour with the Griess-Ilosvay Reagent, consisting of Sulphanilic Acid and α Naphthylamine in Acetic Acid, or by means of the following test (Allen, 5th Edition, Vol. I., 579). The reagent is prepared by dissolving 1 Gm. of Sulphanilic Acid in 100 Cc. of hot saturated Ammonium Chloride solution, and then adding 1.5 Gm. of Phenol and 100 Cc. of 2 N/1 Hydrochloric Acid. The sample of flour, 5 Gm., is macerated with 100 Cc. Distilled Water, filtered and 50 Cc. of the filtrate is mixed with 1 Cc. of the reagent. After 15 minutes, Ammonia (S.G. 0.880) is added and the liquid stirred. An orange-red colour is produced with nitrites and is proportional to the amount present. Minute amounts, of the order of 5×10^{-6} Gm. HNO_2 in 50 Cc., we find, give a distinct yellow colour. As a simple test for bleached flour, the shaking of about $\frac{1}{2}$ oz. with 2 oz. of Petrol, the liquid taking up a yellow colour unless the sample has been bleached, is well known.

According to Kenwood (Public Health Lab. Work), *when over 1.5 parts of nitrites per million are present it may be presumed that the flour has been bleached.* The very slight reaction for nitrites given by all the samples we examined, including a known pure specimen, is probably due to the fact that, as stated by Allen, unbleached flour frequently absorbs small portions of nitrites from the air, especially in industrial towns. At any rate, it is known that even unbleached flour gives a slight nitrite reaction.

The Petrol test does not seem to give conclusive evidence. Thus, although a colourless extract denotes thorough bleaching, there appears to be the possibility that a dark flour might be just sufficiently treated to render it normal in appearance. A very pale Petrol extract, with absence of nitrites, may also be indicative of the use of other bleaching agents, such as Halogens or Ozone.

The data we obtained in 1925 indicated that the sale of bleached flour is widespread.

Bleaching of inferior flours by Nitrogen Peroxide should be stopped. The only persons who profit are the miller and the baker, for from a health point of view it is very questionable.—R. King Brown, Pr., Mar., '26, 272.

Bleaching agents are both unnecessary and undesirable—a part from probable inimical effects on health, their presence serves to lessen, through oxidation, the amount of active Vitamin in bread.—S. G. Willimott and F. Wokes, L. ii./28, 673.

To detect Flour bleached by Chlorine. The Chlorine apparently occurs in or with the extractable fatty matter, being readily soluble in the usual fat solvents. Best extracted by shaking the flour with a mixture of Alcohol, Ether and Petroleum Ether.—Analyst, '26, 150.

Foreign mineral matter may be shown by shaking the sample with Chloroform; the flour floats and the mineral matter separates and may be estimated.

Copper Sulphate, probably employed to prevent or destroy fungoid growth in the corn, has been detected in flour and bread.—Kenwood.

Moisture in Flour.—This should not exceed 15%—Kenwood.

Bread-making.

Wheat and rye are the only suitable cereals for bread-making—owing to the fact that they contain the protein “gluten” which becomes viscid on mixing with water—hence forming a dough. Gluten is developed by interaction in the presence of water of the two proteins gliadin and glutinin.

In wheat flour there is more gliadin than glutinin. Generally speaking, gliadin gives tenacity and elasticity to the gluten, while glutinin gives it strength, and the two proteins must be present in proper proportions if the gluten is to have the properties required in bread-making. In order to make a large light loaf of bread the flour should have a fairly high gluten content, containing a large proportion of gliadin.—H. C. Sherman, Food Products, (1924).

It is of interest to add the following “recipe” used in home baking (since the advent of ‘German’ yeast).

Recipe for Making Bread of the '80's.

Put into a large earthenware jar 6 or 7 lbs. of best flour with a little salt, and allow to stand near the fire. At the same time crumble 1 oz. of German yeast into a gill of luke-warm water and *milk*, into which has been stirred two tablespoonfuls of flour and one of moist sugar. Mix well and then place near the fire to rise. In another basin pour over a little bit of butter or lard

quite a gill of boiling water to "dissolve" it, and when the yeast has risen to the top of the basin make a deep hole in the centre of the flour and after cooling down the water and fat with a *pint of milk* and adding some more warm water, pour into the hole along with the yeast, stirring in some of the flour until it is a pool of batter (with a wooden spoon). Dust a little flour on top and place near the fire to rise. Cover over with a cloth and let it rise up well, then stir up with the flour, adding as much water as will make it up to a medium consistency of dough—*not stiff*,—*kneading it well*, as that makes it light and spongy. Then place it near the fire to rise. Sprinkle a little flour on the top and cover with a heated plate, as that keeps it at a regular, even heat, and it possibly rises better by so doing. Turn the jar round occasionally, so as not to get it too warm one side, and when it rises up again, in rather more than $\frac{1}{2}$ hour, make it into 6 loaves, having your tins warmed and floured, and let it stand quite $\frac{1}{2}$ hour, kneading the loaves well again. Prick well with a fork and bake 40 minutes or $\frac{3}{4}$ hour in an oven not too hot. Two things are necessary, viz. *kneading well* and not having too warm in summer. It must be made warmer in winter, being careful not to scald the yeast. Use rather more than 1 oz. of yeast to 6 lbs. of flour, using less in summer than in winter.

Modern Baking.

Baking to-day, and the flours used, depend on the procedure. The flours are divisible thus:—

- (a) A flour for the "long sponge" method of panification. This takes about 12 hours. "Panification" is virtually the name given to the process of preparing the dough for the baking.
- (b) A flour for the "short sponge" method, where a larger amount of yeast is used and the fermentation conducted at a higher temperature, so as to hasten the process.

Other types of flour are wanted for pastry, buttermilk bread, wholemeal flour, home baking, etc.

General Survey.

To survey a subject regarding which medical authorities, analysts, millers, bakers, and the public have been unable to formulate a regime after years of discussion, is difficult.

Wholemeal Flour and Bread.—The removal of the whole of the bran layer which contains so large a proportion of salts, and which may be deemed "bone-forming" constituents, and the germ rich in protein and fat, appears to be an erroneous proceeding. Physiologists have not been able to agree about it. Extreme advocates on one side say the whole grain flour contains all the nutriment and that the white bread has nothing left in it, while the opponents of wholemeal bread appear to rely on the contention that 'offal' and the parts of the grain until now given to swine, etc., are not digestible by human beings—especially delicate children. It seems to be generally agreed that *wholemeal flour and bread are of value to children and to all who digest them with ease. In such it is not proved to be injurious, on the contrary, it is in some cases the more desirable food.*

The 'roughage' effect of the particles of cellular matter prove beneficial, e.g., in habitual constipation. Occasional consumption of wholemeal bread is certainly desirable and many benefit from its

daily consumption. Much may be left to the dictates of nature. The coarser wheat products in it stimulate peristalsis; the oil of the germ, and *Phytin*—a Phosphorus compound, especially abundant in the bran—may also exercise this effect.

We carefully avoid the phrase 'brown bread.' Brown bread, as found in shops to-day, is often merely a mixture of white flour and coarse bran, and this makeshift is unsatisfactory.

A lot of the whole wheat bread is harmful and unfit for food. A proper balance of fruit and vegetables with bread is the essential factor, as not even wholemeal bread supplies nearly enough mineral matter for the needs of the body.—D. R. Hodgson, *Modern Miller*, 1925.

Stone-milled flour *quickly becomes musty owing to the retention of the "oil"* of the grain, present in the germ and inner coat, *i.e.* the very parts containing the nourishment, while American flour will keep for months, owing to the fact that the highly nutritious parts have been carefully removed and only the starchy elements retained.—A. O. Ward, *B.M.J.* i./24,839. Difficulty of popularising whole-wheat bread.—S. H. Belfrage, *ibid*, 839.

Wholemeal flour is not well adapted to general or continuous use. It does not make good pastry, does not keep well, and soon palls on the appetite. Millstone bread (defined at the commencement of this chapter) recommended as enjoyable and economical.—C. E. Shelly, *B.M.J.* i./24,883.

The majority of the bread eaters of the world (over 94%), prefer bread made from flour derived from the endosperm of wheat only, which means that they demand *White Bread*, with the elimination of the bran, parenchymatous tissue and the germ.

The Miller's and the Baker's Problems.

Hard Flours and Blends with Soft Home Produce.

Our climate produces a wheat containing an excess of moisture, and the dough made from it, as the bakers say, 'does not sit up,' hence the habit of baking in tins, or the addition of the drier Australian or Indian flour.

The use of blends of wheat from overseas with English wheat is excellent, but the net result we regret is that the appetising loaf is seldom found in our cities to-day.

The Public Attitude towards the loaf is, in great measure, exceedingly tolerant, providing it is nice to look at. It is a curious fact that the consumer in the South of England is in no way fastidious. He can be served with a low grade flour and the bread made from it. On the other hand, the South Wales operatives, who are large bread eaters, demand the finest grade. These two pieces of information came out in evidence before the **Departmental Committee on "Treatment of Flour with Chemical Substances,"** which was sitting at the time our last Edn. was in the press.

The information fits in almost exactly with our own observations.

The following we cull from the Report (issued 1927):

Improvers are a great aid to home millers in competition with overseas supplies, enabling them to use any supply of sound wheat available, and thus produce a standard flour at lowest prices. It is admitted this may result in the greater use of commercially inferior wheats, but these are not necessarily less nutritive. (? W.H.M.) Bleaching allows millers to lift 'household flour' into the 'patent' grade. So long as a great demand exists for very white breads (It doesn't.—W.H.M.), some form of bleaching process must be permitted, but **Chlorine, whether free or combined with Nitrogen, and Benzoyl Peroxide, are undesirable additions to Flour.** Not prepared to recommend complete elimination of bleaching

agents and improvers now in use, but it should be made compulsory on **manufacturers to declare to purchasers the precise ingredients**, and compulsory on **millers to inform customers whether flour has been bleached or improved**, and if so, **with what** substance and in what proportions. Welcome possibility of improving flour by physical rather than chemical methods. (We accord heartily. —W.H.M.)—Report of Dept. Cttee. on Treatment of Flour with Chemical Substances, Ref.—L. i./27,609. **Bread of perfect color can be made from unbleached flour.**—W.H.M.

We have had the impression, accumulated during some years, that bread and allied foodstuffs available in London, and other busy centres, are not so appetising as, or of a flavour equal to, similar products supplied in less busy localities, *e.g.* country towns. Bluntly, we always remark, as no doubt do thousands of others, on the excellence of bread, etc., in the North of England. *Why is this?* The inference is that the discriminating purchaser gets the quality he expects. The Lancashire and Yorkshire mill-hand would not be content with the average quality of bread, cakes, etc., supplied in many London shops. The Londoner seems content to put up with *any* type of bread supplied to him. Apparently the floating, cosmopolitan population does not need the same careful handling by the purveyor.

Unfortunately, it is not possible to distinguish one blended flour from another by comparing simple chemical figures for either carbohydrates, protein, fat, ash, water, etc., or several of them collectively. The nature of the protein has to be examined and the simplest procedure of all is the Baking Test.

As a fact, baking experiments (having however no reference to the subject of bleaching) were kindly conducted for us (May, 1925), in the course of this investigation, by authorities interested in the milling industry. Briefly, our examination of numerous specimen loaves showed that a loaf made from a dough panified with yeast was excellent and it retained its moisture far better than those made (a) with buttermilk and requisite added acid and Sodium Bicarbonate, (b) with *milk* and water and additions of Sodium Bicarbonate and Acid Phosphate, (c) self-raising flour containing Sodium Bicarbonate and Acid Salts only.

The yeast loaf was palatable for a week. It seemed probable from these data that bread could be made by using modern self-raising flour only (*i.e. sine yeast*) and that the procedure may be a commercial proposition for a 'quick' trade, but we are told it is not carried out by bakers.

Bleaching and Improvers.

To formulate an opinion on the advisability or permissibility of Bleaching, one may take a few factors. It is *possible* that by allowing bleaching the consumer gets the benefit of a cheaper loaf than if it were prohibited by law (a larger quantity of flour being rendered available for use), but we are *not in favour* of bleaching, and we know that millers who bleach now would gladly drop it if commercial circumstances permitted them to discontinue the practice.

It is probable that 3 parts per million of nitrites, expressed as Nitrous Acid, will be evidence of bleaching. (In some Australian States, it is recognised that the presence of 2 parts per million of nitrites indicates bleaching, and flours containing more than 5 parts per million are condemned.)

We ourselves cannot see any reason why a flour, sold to a purchaser entirely uninformed of the circumstances, should be either untreated or else bleached or chemically "improved" at the discretion of the vendor.

Our Personal View of the Modern Loaf.

The tendency to-day is to provide food of appetising appearance; in many instances this is done at the expense of its nutritive properties. We suggest that the ideal loaf for general consumption is one agreeing with the qualities one recalls years ago—slowly-matured, providing nutritive yeast products, reasonably aerated, of satisfactory weight rather than volume, baked almost black (to yield the purifying effects of carbon), with a quarter-inch crust; a loaf that would keep moist a week, always appetising, made of a good white flour untouched by chemicals, and a truly 'self-raising' dough, capable of synthesising brain, brawn and muscle.

Though well known old-fashioned bread, guaranteed to be made of unbleached flour and including English grown wheat, with no added chemicals whatsoever is now being advertised it would appear that the average individual who only commenced to eat bread within the last thirty years does not know the flavour of old English bread. The loss is to be regretted, but perhaps in the circumstances, he should be congratulated.

[P1] NUX VOMICA (B.P.'14).

CAFTEO-TANNIC ACID thought to be responsible for the blue colour formed in a Tinct. Nucis Vomica and Ammonia mixture—not copper.—F. G. Hobart, P.J. i./24,670; ii./24,159,191. See our Vol. I., p. 599.

Assay Methods.

B.P.'14 requires 1.25% Strychnine. U.S. X. requires 2.5% Total Alkaloids.

The F.I. Alkaloidal strength of powdered drug is 2.5%. Standardisation for total alkaloid does not limit the content of strychnine.

A menstruum of Amyl Alcohol 1, Chloroform 3, and Ether 4 is a useful solvent for the alkaloids in assaying.—A little Amyl Alcohol added to the Strychnine residue prevents decrepitation in drying.

By using Nitric Acid Sp. Gr. 1.435 containing 1% Nitrogen Peroxide, the Brucine is destroyed in a mixture of the alkaloids in 15 minutes.

In the estimation of Strychnine in presence of Brucine, D. B. Dott found the Nitric Acid (Gordin's process) should be allowed to re-act at ordinary temperature for 20 minutes, and higher temperature should be avoided.

Benzol (B.P. '98) is not such a good solvent for Strychnine as Chloroform but is advised in preference to the latter if used in larger quantity for extraction in the estimation process; it does not emulsify.—H. Deane, P.J. ii./24,96. See also D. B. Dott, *ibid* 251.

Strychnos cinnamomifolia from Travancore. Total alkaloidal content from 2.432 per cent. to 2.801 per cent., only about 0.3 per cent. being strychnine. The seeds closely resemble those of *S. Nux vomica*, but have not been commercially exploited.—G. R. A. Short, B.P.C. 1924.

Extractum Nucis Vomicae Liquidum (B.P.' 14.)

B.P. '14—Standardised to 1·5% Strychnine.

In the B.P. '14 assay method the brucine is entirely destroyed by the nitric acid in ten minutes by heating to 50° C.

Toxicology.—It is useful to Extract with Acetic Acid and Alcohol. The Alcohol assists filtration.

Cold nitration of the Brucine with *active* nitric, or acid rendered so by adding Sodium Nitrite essential. "50° Nitrations" cause large percentages of error (loss). Gravimetric results supply erroneous deductions. Strychnine Nitrate is an anomalous salt to deal with by the process of immiscible solvents. Differences between standardised extracts of commerce were found of 10·5%.

—H. R. Jensen. P.J. ii./16,458.

Spectrum of Strychnine.—The smallest quantity, *e.g.*, 1/500 grain, can be detected—useful in cases of poisoning. Alkaloids generally give characteristic spectra.—The late Prof. J. J. Dobbie.

There is evidence of a further alkaloid in Nux Vomica apart from Strychnine and Brucine.—C. A. Hill, Pres. Add. B.P. Conf., 1920.

Volumetric estimation of Liq. Strychninae, using N/10 Potassium Bichromate, which precipitates the alkaloid quantitatively from slightly acid solution. —J. Rac, P.J. i./28,270.

OLEA ESSENTIALIA.

"The History and Chemical Relations of the Terpenes."—One of a series of Post Graduate Lectures at the Pharm. Soc., by Sir W. A. Tilden. Complete report, Perfumery Record, July 9, 1912.

Synthesis of the Terpenes.—Prof. Perkin, *ibid.*

For the extraction of perfumes by distillation, solvent, etc., various methods are in use. For **cold enfleurage**, as used for Jasmin and Tuberose, a mixture of pork and beef fat is used. **Warm enfleurage** can be used for the more stable Essential Oils, *e.g.* Rose, Cassia and Violet. Petroleum Ether is also largely employed, *e.g.* for Violet. On removal of the solvent the so-called **Concretes** are obtained, *i.e.*, oils + resins, fats, colouring matter, etc.—these by-products have to be removed to produce the "**Absolutes**."

Enfleurage process, Petroleum Ether and other processes described in an article on the Riviera Perfumes.—C.D. i./27,319.

Absolute Flower Oils—a comparison of the enfleurage and volatile solvent products, with description of the enfleurage process.—W. A. Poucher, C.D. i./28,308.

Sources of Various Oils.—Island of Reunion yields Geranium Oil. Mexico.—Linalce Oil. French Guiana.—Bois de Rose Femelle (for producing lily of the valley odours). Philippine Islands and Madagascar.—Ylang Ylang. Java, Burmah and Uganda.—Citronella Oils. This latter oil is now used for making various artificial violet bodies.

Saponification process for Esters in Essential Oils and **Acetylation process** for alcoholic constituents, also methods for determining **Refractive Index** and **Optical Rotation**, are briefly dealt with in the B.P. appendices.

The principal methods employed in the **analysis of perfumery and flavouring synthetics** and isolates, with results for pure samples, are described in a treatise by T. H. Durrans,—P.R. '24,210.

Refractive index of liquids, instrument for.—R. Fouracre, P.J. ii./22,88.

Tables of the more common fatty oils and essential oils, showing Sp. Gr., Iodine Value, Saponification Value, and Refractive Index.—C.D. i./28,366.

Terpeneless Essential Oils.

Essential Oils, deprived of their Terpenes and Sesquiterpenes, which in many instances constitute a large proportion of the Oils, have the advantage of being *stronger in flavour and perfume* than the natural Oils and are much more readily *soluble* than the latter.

TERPENELESS ESSENTIAL OILS. (From P.R., July, 1921).

	Concentration.	Sp. Gr.	O. R.	R. I. (25°).	Solub. in Alc.
Anise ..	1½	.982—.984	0 to — 1°	1.553—1.554	1 in 1 (90%)
Angelica	20	.975—.980	— 1° to + 1°	—	—
Bay ..	2	1.025—1.045	0 to — 1°	1.526—1.528	1 in 2 (70%)
Bergamot	2½	.885—.890	— 6° to — 10°	1.455—1.457	1 in 1 (80%)
Calamus	3	.900—.915	— 8° to — 20°	—	—
Cananga	5	.900—.915	— 8° to — 20°	1.486—1.488	1 in 1 (95%)
Cardamoms	2	.943—.956	+ 33° to + 46°	—	—
Caraway	2	.960—.964	+ 58° to + 60°	1.495—1.497	1 in 2 (70%)
Celery ..	8	1.015—1.080	— 40° to — 60°	1.500—1.505	1 in 2 (85%)
Citronella (Ceylon)	2	.910—.930	— 2° to — 5°	—	1 in 2 (70%)
" (Java)	1½	.880—.900	— 1° to + 1°	1.470—1.472	1 in 2 (70%)
Cloves..	1½	1.060—1.070	Nil	1.534—1.538	1 in 3 (60%)
Coriander	1½	.877—.881	+ 8° to + 10°	1.463—1.465	1 in 3 (65%)
Cumin	—	.965—.975	+ 4° to + 8°	—	—
Dill ..	2	.960—.965	+ 52° to + 62°	1.488—1.489	1 in 1.5 (75%)
Galangal	—	.940—.950	— 3° to + 3°	—	—
Ginger..	10	.880—.890	+ 10° to + 28°	1.471—1.486	1 in 1 (90%)
Hops ..	8	.935—.950	— 1° to + 1°	—	—
Juniper	5	.935—.965	— 4° to + 4°	1.500—1.508	1 in 1 (90%)
Lavender	2½	.895—.905	— 7° to — 9°	1.458—1.460	1 in 2 (70%)
Lemon..	20	.893—.899	— 5° to — 9°	1.479—1.481	1 in 1 (80%)
" Sesquiterpeneless	25	.900—.905	0 to — 3°	1.479—1.481	1 in 3 (70%)
Limes ..	15	.918—.925	— 1° to — 6°	1.479—1.481	1 in 1 (80%)
Neroli..	2	.885—.890	+ 2° to + 6°	—	1 in 3 (70%)
Nutmeg	5	1.010—1.100	0 to + 6°	1.505—1.516	1 in 2 (80%)
Orange (Sweet)	50	.885—.895	+ 8° to + 25°	1.472—1.474	1 in 1 (80%)
" Sesquiterpeneless	65	.900—.905	+ 3° to + 6°	1.474—1.477	1 in 3 (70%)
Peppermint	1½	.905—.915	— 24° to — 30°	1.458—1.460	1 in 3 (70%)
Petitgrain	2	.890—.895	+ 1° to + 3°	1.459—1.461	1 in 1 (80%)
Pimento	1½	1.056—1.064	Nil	1.535—1.537	1 in 1 (70%)
Rose (Stearopteneless)	1½	.882—.885	— 3° to — 5°	1.466—1.468	1 in 1 (70%)
Rose-Geranium	1½	.890—.895	— 7° to — 11°	1.463—1.465	1 in 2 (70%)
Rosemary	5	.925—.960	0 to + 10°	1.470—1.472	1 in 2 (75%)
Sage ..	6	.930—.940	— 5° to + 10°	1.465—1.467	1 in 2 (75%)
Spearmint	4	.950—.964	— 40° to — 50°	1.488—1.490	1 in 2 (75%)

Sesquiterpeneless Oils

As a further refinement' to produce even more Soluble Oils, the removal of the Sesquiterpenes in addition to the Terpenes, is effected. The following data are from a paper by T. H. Durrans (P.R., July, 1924, p.240, *et seq.*) with revisions to date.—1929.

	CON- CENTRATION.	SOLUBILITY IN ALCOHOL.
Absinthe	—	2 to 3 vols. 70%
Angelica	20	3 vols. 70%
Aniseed	1.5	10 vols. 80%
Bay	2—3	1—1.5 vols. 70%
Bergamot	2.5—3	1 vol. 80%; 3—4 vols. 70%
Calamus	—	25 vols. 60%; 3 vols. 70%
Cananga	6	1 vol. 90%
Caraway	2	2 vols. 70%; 19 vols. 50%
Cardamom	2	2—3 vols. 70%
Cassia	—	2 vols. 70%
Cedarwood	—	1 vol. 90%
Celery	8	2 vols. 80%
Cinnamon Leaf	3	1 vol. 70%; 3 vols. 60%
Citronella (Ceylon)	2	2 vols. 70%
Citronella (Java)	1.5	2 vols. 70%
Cloves	1.5	2.5 vols. 60%; 1 vol. 70%
Coriander	1.5	2 vols. 70%
Cumin	1.5—2	5—7 vols. 70%
Dill	2—3	2—3 vols. 70%
Eucalyptus Globulus	2—3	2 vols. 70%
Fennel	1.5	1 vol. 90%
Geranium	1.5—2	1—2 vols. 70%
GINGER	—	2—4 vols. 70%
Hops	8	1 vol. 80%; 20—30 vols. 70%
Juniper	4	1 vol. 90%
Lavender (French)	2	1—2 vols. 70%
Lemon	25	3 vols. 70%
Lemongrass	—	2 vols. 70%
Linaloe	1.5	1.5—3 vols. 70%
Limes (Hand-pressed)	6	2 vols. 70%
Limes (Distilled)	15—20	1.5 vols. 70%
Mandarin Orange	70	2.5—4 vols. 70%; 1.5 vols. 80%
Marjoli	2	2—2.5 vols. 70%
Nutmeg	5	1 vol. 80%; 4 vols. 70%
Orange	65	2—3 vols. 70%
Palmarosa	1.5	2 vols. 70%
Pennyroyal	2	2 vols. 70%
Peppermint (American)	2	3 vols. 70%
Peppermint (Jap. dementholised)	2	2.5 vols. 70%; 6 vols. 60%
Peppermint (Mitcham)	2	2.5—3 vols. 70%
Petitgrain	2	1 vol. 80%; 3 vols. 70%
Pimento	1.5	1 vol. 70%
Pinus Sibirica (Abies)	2—3	3 vols. 70%
Rosemary (French)	2	2—3 vols. 75%
Rose Otto (Stearopteneless)	1.5—2	1—1.5 vols. 70%
Sage	6	2—2.5 vols. 75%
Sandalwood	1.5	3—5 vols. 70%
Sassafras	—	1 vol. 90%
Spearmint	4	2 vols. 75%
Spike Lavender (French)	2	2 vols. 70%
Spike (Spanish)	1½	2 vols. 70%
Thyme	2—3	2—3 vols. 70%
Tetivert	10	1 vol. 80%
Tlang (Manilla)	4—5	1—1.5 vols. 90%

It is doubtful whether an oil containing very delicate esters, *e.g.*, Bergamot oil, is improved by removing the terpenes. Further, there is no point whatever in rendering terpeneless an oil consisting almost entirely of its odorous constituent such as Clove Oil.

Lemon Oils from which the terpenes only have been removed contain in the neighbourhood of 42 to 45% Citral, whilst those from which the sesquiterpenes have also been taken contain up to 65%, or, as claimed by some makers, 72% Citral. The removal of the sesquiterpenes, in addition to the terpenes, causes the Oil to lose the sweetness and softness of a well-made terpeneless oil. Some users hold that the best results are obtained with an Oil containing under 40% Citral from which the whole of the terpenes have not been removed.—E. J. Parry, C.D. ii./13,378.

Lemon Grass Citral, now purified to such an extent that the Verbena odour is completely removed, is possibly used to adulterate Sesquiterpeneless Lemon Oil. It will be seen from the following—

Sesquiterpeneless Lemon Oil,	Sp. Gr.	0.895,	Rotation 0° or to 1°, Citral 65%.
Terpeneless Lemon Oil,	Sp. Gr.	0.895,	„ -3 to -4°, „ 45%.
Citral,	Sp. Gr.	0.895,	„ 0°, „ 100%.

that it is possible to add to 100 parts of Terpeneless Lemon Oil 80 or 90 parts of Citral to produce a Sesquiterpeneless Lemon Oil differing only by its rotation of -2.—*See also Oleum Limonis Chapter.*

Indian Essential Oils.—**Lemon Grass Oil** is one of the chief oils distilled on the West Coast, but there is room for improvement in manufacture. The night-flowering plants of India may yield possibilities.—C.D., 1920, p. 1435.

Practically all Lemongrass Oil is of East Indian origin, and is obtained from *Cymbopogon flexuosus*, the Malabar or Cochin Grass. The oil is sold on its Citral value. The principal use of Lemongrass is for extraction of Citral for the manufacture of Ionone. The oils giving the largest Citral content are those from Ceylon 76, Cochin 84.5, Mayotte 87, and Seychelles 76-81.—C.D. ii./27,161.

African Essential Oils. Reports on Geranium Oil, Oil of *Pittosporum undulatum*, South African and Rhodesian Fennel Seed and S. Rhodesian Dill Seed oils.—C.D. ii./27,126.

Synthetic Perfumes.—For a synopsis of the principal bodies used in making synthetic perfumes *vide* Pharm. Formulas, 1914, and Perfumery Record, July 5, 1914.

Solubilities of perfumery ingredients, essential oils and synthetics, in Ethyl Alcohol, *see* Table.—P.R. '24,283.

Carminative Volatile Oils applied to mucous membrane in dilute solution increase muscular movements in the intestine in dogs. Effects lessened by Atropine.—O. H. Plant, Jl. Pharm. & Exp. Therap., Nov. 1920.

ANTISEPTIC POWERS OF ESSENTIAL OILS.

We determined the "*Lancet*" Carbolic Acid Coefficient (using *B. Coli Communis*), of the more important Essential Oils and aromatic substances.

A paper, P.R., Nov. 1910, provided the minimum lethal strengths, using Aqueous Solutions with 2 and 30 minutes contact, and the minimum lethal strengths with Saponaceous Solutions (diluted at time of use to form emulsions). From these the CARBOLIC COEFFICIENTS were obtained by stating the comparative strength with Phenol Solution. In other words by dividing the M.L.S. (Minimum Lethal Strength) as compared with unity of the Essential Oil Dilutions by the M.L.S. as compared with unity of the Phenol Dilution we obtained Coefficient figures at respectively 2 and 30 minutes—(100 and 170 respectively were the M.L.S. for Phenol)—the mean of the two results is the Carbolic Acid Coefficient.

The antiseptic power of many of the Oils cannot be determined by Aqueous solution as a saturated aqueous solution is not strong enough to kill the test organism: the Saponaceous Solutions overcome the difficulty.

The Coefficients show that several of the Oils possess considerable antiseptic power. The two isomeric monatomic phenols, Carvacrol and Thymol homologues of Phenol (acknowledged valuable antiseptics)—disputing the premier position in the table, have almost the highest molecular weights of those occurring in the commoner Essential Oils.

The Oils might produce different Coefficients if other organisms were employed. *See recent work later.*

As an outcome of this investigation Saponaceous Solutions of some of the Essential Oils are prepared for physicians' use under the name **Perfumed Formosyls**, *vide Vol. I., p. 600.*

The results were briefly as follows:—

ANTISEPTIC POWERS OF ESSENTIAL OILS.

Essential Oil Dilution.	C.A.Co-efft	Chief Chemical Constituents.
<i>Origanum Oil (A.)</i>	26	82% Phenols, <i>e.g.</i> , Carvacrol.
<i>Thymol (S.)</i>	25	—
<i>Carvacrol (S.)</i>	21	—
<i>Thymol (A.)</i>	19	—
<i>Thyme Oil (S.)</i>	15	46% Phenols (Thymol, &c.)
<i>Thyme Oil (A.)</i>	13	<i>As above.</i>
<i>Geraniol (S)</i>	12	—
<i>Cinnamon Leaf Oil (S.)</i> ..	10	86% Phenols, <i>e.g.</i> , Eugenol.
<i>Cinnamon Bark Oil (S.)</i> ..	9	52 % Aldehyde, <i>e.g.</i> , Cinnamic.
<i>Clove Oil (S.)</i>	9	90% Phenols, <i>e.g.</i> , Eugenol <i>v. ante.</i>
<i>Cinnamic Aldehyde (S.)</i> ..	8	—
<i>Citronellol (S.)</i>	8	—
<i>Cinnamon Bark Oil (S.)</i> ..	8	82% Aldehyde (Cinnamic Aldehyde).
<i>Cinnamon Bark Oil (A.)</i> ..	7	82% Aldehyde.
<i>Rosemary Oil (S.)</i>	6	—
<i>Otto of Rose (S.)</i>	6	68% alcohols estimated as Geraniol.
<i>Cassia Oil (S.)</i>	5	83.5% Aldehyde (Cinnamic).
<i>Wintergreen Oil (S.)</i>	5	Methyl Salicylate.
<i>Eucalyptus Amygd. (S.)</i> ..	5	Phellandrene and Eucalyptol.
<i>Lavender Oil (English) (S.)</i>	5	Esters as Linalyl Acetate $\text{CH}_3\text{COOC}_{10}\text{H}_{17}$, 11%. Linalool is isomeric with Geraniol. Other constituents of the oil are Linalool as such, Esters, other than the Acetate, Cineol and Limonene.
<i>Lemon Oil (S)</i>	4	Limonene, Citral 4 to 7% Citronellal, Geranyl Acetate, possibly other esters of Geraniol and Citronellal.
<i>Almond Oil, Ess. S.A.P. (S.)</i>	4	Benzaldehyde chiefly.
<i>Eucalyptol (S.)*</i>	4	—
<i>Eucalypt. Glob. Oil (S.)</i> ..	4	67% Eucalyptol together with Pinene, Phellandrene, Alcohols and Aldehydes.
<i>Garlic Oil</i>	2	Allyl Sulphide chiefly.
<i>Light Oil of Tar (Rect.) (S.)</i>	2	Volatile Bodies. Contains no Phenols.
<i>Santal Oil (S.)</i>	1½	Contains 93.8% Alcohol calculated as Santalol $\text{C}_{15}\text{H}_{23}\text{OH}$.
<i>Birch Tar Oil (S.)</i>	1½	Stated to contain Guaiacol, Cresol and Pyrocatechin.
<i>Cade Oil (S.)</i>	1	—

A = Aqueous Solution. S = Saponaceous Solution.

**Eucalyptol*.—G. I. Hudson has found the C.A. coefficient to be 4.4.

L. Cavel (*see P.R.*, September 1918) came to similar general conclusions. He also places **Thyme** and **Origanum** Oils first and the order in his list is in agreement with our own.

Affinity of Phenols for Bacterial Protein.

Certain substances, *e.g.* Formaldehyde, have a direct interacting power with Protein. In the case of the Phenols and Cresols the action is more complex and a theory has been set up on the lines of an upheaval of the colloidal elements of the bacterial body and consequent formation of an irreversible substance. The precipitated protein is not again dispersed. The action is in short very similar to that of heat—as in the case of heating egg albumen.

Bringing this to bear upon the Essential Oils we see that the Oil heading the list contains 82% of Carvacrol or allied Phenol and that the substance is

practically as strong as is the phenolic Thymol which is isomeric with it. Then follows Thyme Oil with 46% Thymol and subsequently Cinnamon Leaf and Clove Oil containing 86% to 90% Eugenol (or allied bodies). A little lower comes Cinnamon Bark Oil (82% Aldehyde).

In short we have in these preparations, *especially in the minute subdivisions effected in Saponaceous Emulsions just the very bodies—higher up in the homologues series* which were known to be markedly antiseptic. The two isomeric PHENOLS which rank highest in our experiments have almost the highest molecular weights of those occurring in the commoner Essential Oils—far higher than Phenol or the Cresols, herein is doubtless an answer to the question of how the Essential Oils act. To introduce the colloidal theories would not appear to greatly assist the matter. **We should ascribe the effects to one analogous with that of the caustic action of Phenol on the tissues—a direct combination with protein.** Bacterial protein may be particularly responsive to these antiseptic oils.

Numerous other workers have followed up our investigations on somewhat similar lines:

The Carbolic Acid Coefficients, using the *Lancet* method, determined for a large number of essential oils and synthetics. The results, confirming Martin's original work, support contention that *perfume materials have a germicidal value equal to the best disinfectants.*—J. J. Bryant, P.R. '24,252.

The Rideal-Walker Coefficients of some essential oils—chiefly Australian—and their pure constituents.—P.R. '24,127,388.

Recent work by S. Rideal, E. K. Rideal and A. Seiver produced results similar to those obtained by us in 1910. Using the Rideal-Walker method with *B. typhosus* as the test organism, they obtained an order of germicidal power for Cinnamon Leaf, Clove, Cassia, Eucalyptus, Lavender, and Lemon Oils, practically identical with our values.

A 20% emulsion of the oil in 6% **Green Soft Soap solution** was used in each case, the results being liable to an error of 5 to 10%. Generally it was found that those oils with a high germicidal power formed stable soap solutions.

It was shown that a relation can be established between the power of oils to lower interfacial surface tension and their germicidal activity, the general rule being that **oils of high Carbolic Coefficient are more likely to lower surface tension.**

Tables are also given showing the R.W. Coefficients of Essential Oils and their constituents by A. R. Penfold and R. Grant.—P.R. '28,285.

Bactericidal action upon Catarrhal Organisms.

The following values were obtained for the Carbolic Acid Coefficient on some commercial perfumes, using a mixed culture from the nose, *Micrococcus catarrhalis* preponderating as the organism, and making the dilutions of the perfumes with 5% solution of rosin soap.

Carnation has a Coefficient of 0.62, Lily of the Valley 0.1, Jasmin 0.15, Heliotrope 0.16, Opoponax 0.18, Lilac 0.09, Narcissus 0.1, Night Stock 0.4, White Rose 0.45, Sweet Pea 0.045, Wallflower 0.12 and Violet 0.11. Many similar results stated, show that perfumes have a distinct bactericidal value. The replacement of some of the spirit in the perfume by Isopropyl Alcohol in general, slightly increases this bactericidal power.—F. C. Dyche-Teague P.R. '24,6,40 81.

At 37°, the vapours from Bergamot, Caryophyllum, Cinnamon, Citrus microcarpus, Eucalyptol, P. Sylvestris and Turpentine **prohibited growth of tubercle bacilli**, and it is stated that the volatile constituents of some oils show high disinfecting activity, with indication of **selectivity towards acid-fast bacteria.**—P.R. '24,330.

The addition of perfume materials to soap adds considerably to its germicidal powers.—J. J. Bryant, P.R. '24,426.

Essential oils provide the best means by which the TEETH AND MOUTH may be kept healthy—formulae of some dentifrice preparations given.—P.R. '24,49.

The Odorous Principles of Plants.—F. B. Power, C.D. '19,971,1003. See also J.C.S.A. i./19,607.

OLEUM CITRONELLÆ.

Genuine Oil from Ceylon Government gave the following figures: Sp. Gr. at 15.5° C., 0.884. Optical rotation—3.3, Citronellal 36%, Geraniol 11%.

Citronella Oil with Carbolic Acid acts admirably in driving off mosquitoes. (Cairo).—Ph. Notes. Bamber Oil contains this and Kerosene, *v. Malaria*.

The tse-tse fly was thought to have marked repugnancy to the plant (*cf. trypanosomiasis*) but it has lost its reputation as a means of warding off the insect—the odour of the oil is not given off without bruising the plant.

Citronellol and Citronellal. Formylation Method unreliable.—C. T. Bennett, P.R., 1921, 12,351, Y.B.P., 1922, 66.

Citronella Oils having refractive index of 1.472—1.473 have contained 6 to 8% of *Ethyl Alcohol as adulterant*, normal R.I. being 1.479—1.482. The Alcohol should be determined in the ordinary way since it would not be indicated by acetylising method of estimation, the Ethyl Acetate formed dissolving on washing the acetylated oil.—E. J. Parry, C.D., Sept. 15/23, 390.

OLEUM EUCALYPTI (B.P. '14).

(See also Vol. I., p. 613, et seq.)

Sources and characters of Eucalyptus Oils.

The work entitled "RESEARCH ON THE EUCALYPTUS, ESPECIALLY IN REGARD TO THE ESSENTIAL OILS," by R. T. Baker and H. G. Smith, 2nd Edn. 1920, by authority of the Government of New South Wales is the standard work on the subject and should be consulted by all requiring further information.

Eucalyptus and other Australian Essential Oils. Conditions of the industry. *E. Macarthuri* yielding from 60 to 75% Geranyl Acetate is much in favour. —C.D. '20, 746.

Description of oils of *E. polybractea*, *E. phellandra* (formerly *amygdalina*), *E. dives*, *E. Macarthuri*, *E. citriodora*, *E. cneorifolia* and others.—A. B. Penfold, P.R., 1922, 324, Y.B.P., '23, 101.

Eucalyptol. Syn. Cineol, Estimation

The Phosphoric Acid Method may be used as B.P. '14 in Oleum Eucalypti. It is more accurate than the Resorcinol method—the latter gives results far too high.

U.S. IX. assayed by converting the Eucalyptol into Arsenate at 0° C. The Arsenate is pressed out and split up by means of hot water and read off by volume. U.S. X. requires 70% Cineol, but method of Assay is not now given.

Dodge suggests destroying the Terpenes with cold 5% Potassium Permanganate Solution and after 24 hours contact dissolving the Manganese Dioxide with Sulphuric Acid and measuring the volume of unoxidised Eucalyptol. C. T. Bennett finds the method works with Oils rich in Cineol, but not with low grade Amygdalina Oil.—P.R., 1912, 276, 295.

If 2 Cc. be mixed with 4 Cc. of glacial acetic acid and 3 Cc. of Saturated aqueous Sodium Nitrite, when gently stirred should not form crystals of Phellandrene Nitrite (exclusion of oils containing much phellandrene)—U.S. IX. has this test modified by addition of Petroleum Spirit.

C. T. Bennett and M. S. Salamon found the most correct result out of numerous modifications tried, is by use of 5 Cc. of Phosphoric Acid in the B.P. '14 method instead of 6 Cc.—P.R. 1919, p. 211.

Arsenic Acid method estimation. It forms an addition compound sufficiently stable for the purpose and the results are accurate within 2%. The Phosphoric, Hydrobromic Acid and Resorcinol methods criticised.—J. L. Turner and R. C. Holmes, P.J. i./15, 60.

α -Naphthol has been suggested as a substitute for o-Cresol in the estimation of Cineol in Eucalyptus Oils (P.R. Jan. '24, 9), *v. Cresineol infra*. This procedure has, however, been criticised.—T. Cocking, P.R., Jan. '24, 10. The method of determination in Essential Oils is based on the measurement of the freezing point and density of a mixture with Naphthol.—G. Walker, J. Soc. Chem. Ind., '23, 42, 497, per J.C.S., A. ii./24, 131.

Amygdalina Oil was deofficialised because it was supposed that the efficacy of Eucalyptus Oil is due to Eucalyptol; but it was pointed out previously that the reputation of the Oil in Europe was based upon the use of Amygdalina Oil.

Phellandrene. $C_{10}H_{16} = 136.128$ is a large constituent of the oil of *E. Amygdalina*. The irritating effect of some oils when inhaled has been attributed to this body, but the more general view is that the Aldehydes produce it. Phellandrene occurs also in the oil of *E. Risdoni* and many others. It is absent from the oil of *E. Smithii* and oils of that group.

Parry reported cases of diluting B.P. Oils with *Amygdalina* Oils so as to come just within official limits.

This we think reflects too much on the honesty of the producer in Australia. Formerly the leaves of the various species used for distillation were not kept separate with the required care, but the venation of the different leaves as laid down by Baker and Smith has enabled both the gatherers and the distillers of leaves to readily distinguish the different species.

Eucalyptus Oil (*Amygdalina* Var.) is used in metallurgy in treating refractory ores, which are ground with water to which a small percentage of the oil is added, the effect of the oil being to bring the mineral particles to the surface. Enormous quantities of the oil have been consumed in preparing sulphides of zinc and lead. About $\frac{1}{2}$ lb. oil is emulsified by vigorous shaking with about 100 gallons of water, and with this mixture the moistened or powdered ore is stirred. The oil absorbs the sulphide particles and carries them to the surface, together with the gold and silver contained in them, up to 95 per cent. of the actual content of the powdered ore being recovered by the process. "Phellandrene Oils" it is said work better than others and can thus be used up.

Aromadendral $C_{10}H_{14}O$ is the levorotatory high boiling aldehyde found in numerous *E. Oils*. It is a dehydro-aromatic aldehyde discovered by H. G. Smith. It does not occur in the group of oils to which *E. Amygdalina* belongs; the characteristic constituent in this group being Piperitone, a ketone, and the objectionable aldehydes are of low boiling point.—Hudson.

139 species of *Eucalyptus* have been critically revised. *E. Viminalis* and *E. Rubida* yield a kind of manna.—P.J. ii./16,82.

Examination of the Aromatic Aldehydes from *E. Nemiphloia* showed that the so-called Aromadendral is a mixture of Cuminaldehyde and Phellandral in various proportions.—A. R. Penfold, J.C.S., 1922, 121,266, Y.B.P., 1922,67.

* **Cresineol.**—A compound of Cineol with *orthocresol*. It can be made by mixing Eucalyptus Oil with *orthocresol*. Analogous procedure with *meta* and *paracresol* does not produce a crystalline compound, though there is heat evolved. Cresineol has melting point $55.2^{\circ} C.$, Sp. Gr. 0.9661. Readily soluble in organic solvents. It is slowly decomposed by weak alkalis and to a slight extent by water. The formation of the compound can be used as a method for estimating cineol.—T. Tusting Cocking, B.P. Conf., 1920.

Eucalyptus and Cajuput Oil.

The ortho-cresol method for Cineol adopted by Committee on Unification of Analytical Methods. Description of the test.—Y.B.P. '27,114.

See also Ol. Lavand. and Ol. Rosmarini.

Resorcin of course produces a compound. Pyrogallol also makes a compound which crystallises out rapidly. Other phenols tried did not act similarly.—W. H. M.

OLEUM LAVANDULÆ FLORUM.

Volatile oil from *Lavandula vera* (*Labiatae*), has Sp. Gr. usually not below 0.885 up to 0.900 at $15.5^{\circ} C.$ Soluble in three parts of 70% Alcohol. Shaken with water in a narrow graduated cylinder, volume of oil should not be diminished (absence of alcohol) (U.S. X.). Terpinolene (*q.v.*) is an adulterant. English oil should contain from 7 to 11% of esters, and the foreign oil not less than 30% of esters, calculated as linalyl acetate $C_{10}H_{17}C_2H_3O_2 = 196.16$, as determined by saponification with alcoholic potash.—B.P. '14.

This 30% minimum for the foreign excludes some genuine high-grade samples.—Parry. There is no evidence to show that the esters improve the odour or that they have any medicinal value.—Henderson.

Ph. Ital. requires about 35% Linalyl Acetate.

Cineol determination in Lavender, Spike and Rosemary Oils by the Cresineol Method. For oils containing 45% or more of Cineol it is well to proceed thus. 3 Gm. of the oil are mixed with 2.1 Gm. melted Ortho-cresol and the mixture allowed to cool. If no crystals form by the time the temperature drops to $24^{\circ} C.$, the amount of Cineol is less than 45%. 5.1 Gm. Cresineol

s added, and the mixture warmed until liquid, it is then well stirred and freezing-point is determined. The percentage of Cineol corresponding to freezing-point is found by reference to curve, and is corrected for the added Cresineol by subtracting 50 and then doubling the remainder. French Lavender Oil differs considerably, apart from Ester content, from Spike Oil in amount of Cineol present.—T. T. Cocking, P.R., 1921, 12, 339, Y.B.P., 1922, 61.

Suggested that 1 in 4 parts of 70% Alcohol should be the standard of solubility of the French Oil.—Finnemore.

The '**Lavender Controversy**' was started in Germany. It was to the effect that Lavender Oil was valuable in proportion to the percentage of ester. This dictum would have resulted in the total extinction of English oil, which only has about 8 per cent. of ester. The Germans, however, started on an oil about which perfumers knew much, for the latter refused to accept such a standard, and as everyone knows, English lavender oil is pre-eminent.—Guy Radcliffe, C.D., March, 25/22, p. 382.

OLEUM LIMONIS (B.P. '14).

Syn. Oleum Citri. P.G. VI.

From fresh Lemon Peel by expression. 1,000 lemons yield 14—16 oz. of oil. Sp. Gr. 0.857 to 0.860. O.R. not less than + 59°. U.S. X. requires 4% Aldehyde by weight calculated as Citral. It ranges from 4 to 7%. Citral $C_{10}H_{16}O$ = 152.128 is optically inactive. Sp. Gr. 0.893 to 0.897. It occurs in a number of other essential oils. A somewhat extensive investigation by U.S.A. authorities went to show that where pinene is found in Lemon Oil, using ordinary means of distillation, it is *prima facie* evidence of adulteration. Other authorities are, however, of opinion that Pinene is a natural constituent of Lemon Oil. Umney said Pinene may or may not be present. The Nitrosochlorides of other terpenes may be similar to that of pinene.

The oil should not be exposed to light or air and the presence of Lemon Juice also causes deterioration.—Finnemore.

Practically the world's supply is obtained from Sicily. The greater part of the crop contains well over 4% Citral, but a large proportion exported is doctored down with Lemon Terpenes to meet the B.P. minimum standard. Lemon Oil contains over 90% of Terpenes and Sesquiterpenes, the former predominating.—C.D. ii./27, 161.

Freshly expressed oil of lemon has an optical index of +70° to +76°, at 20° C. An optical rotation exceeding 76° indicates an oil which has suffered alteration; this, however, does not apply to terpeneless lemon oils. In a fresh oil the acid value is very low, and an increase of this index is a characteristic of an oil which has been kept for some time. On shaking a sample which has undergone alteration with an equal volume of hydrochloric acid (Sp. Gr. 1.19) for one minute, the acid layer assumes a brownish coloration varying in intensity. The Eibner-Hue-Zahl of normal lemon oil averages 0.6—1.2, the higher figure, in conjunction with a refractive index of the residue exceeding 105°, points to the presence of liquid paraffin or a mineral oil as an adulterant.—C.D. ii./28, 780.

Hydroxylamine Process of estimating Aldehydes and Ketones, with a mixture of Citral, Geraniol, Linalool and Geranyl Acetate, in the proportions in which they occur in 'Sesquiterpeneless' Lemon Oil. The method was shown to be at least as satisfactory as the Sodium Bisulphite Absorption Process for determining Citral in Concentrated Oil of Lemon.—A. H. Bennett and F. K. Donovan, Analyst, 1922, 47, 146. Y.B.P., 1922, 51.

The critical solution temperature in Alcohol of Lemon Oil suggested as a means of detecting Terpene adulterants.—G. Ajon, '24, 294.

P.G. VI. requires that the oil shall be *soluble* clearly 1 in 12 of Alcohol—or to show only a little flocculent matter,—*absence of Fatty Oil and Paraffin*.

Machine processes of extraction will supersede sponge method.—Moore and Bennett, P.R., 1922, 15, 36; Y.B.P., 1922, 71. See also P.R., 1924, 15, 23.

For Lemon Tincture and Syrup and Lemonene, see Vol. I. p. 367.

Terpeneless Lemon Oil Manufacture.

This industry in Southern Italy and Sicily is now a matter of considerable competition, resulting in improvement in the technical details of the process adopted. The Lemon Oil used for the distillation is the finest obtainable owing to the greater yield of Terpeneless Oils obtained. During the past five or six years there has been a marked improvement in the quality of Lemon

Oil produced and considerable quantities testing between 5% and 5·8% Citral are now obtained. These are the qualities which are used for the manufacture of the Terpeneless Oils. About 93% is distilled off in a tin-lined copper still at the best vacuum obtainable, usually between 10 and 20 millimetres. No fractionating column is required as if the distillation is conducted slowly the Terpenes will not contain more than about 1% Citral. The Residue left in the still is steam-distilled and about 5% of Terpeneless Oil is obtained, leaving about 2½% of natural waxes and colouring matter in the still. The Terpeneless Oil so obtained has the following characteristics:

Specific Gravity	0·895 to 0·900
Optical Rotation	- 3 to - 10.
Citral	From 45% to 50%

The only points of importance are that the natural Lemon Oil must be absolutely pure; any impurity in it is bound to affect adversely both the yield and the quality of the final Terpeneless Oil. It is also necessary to keep the vacuum absolutely constant throughout the process, otherwise there is a considerable risk of "burning" the final product.—W. C. Slater, 1925.
See also p. 126.

Sesquiterpeneless Lemon Oil Manufacture.

This industry has now been taken up widely in Sicily as well as in other countries. The usual characters given by a Sesquiterpeneless Lemon Oil (one part of which equals in flavour 20 to 30 of natural oil) are:

Specific Gravity	0·895
Optical Rotation	0 to -1
Citral	65%

Solubility.—The oil has the advantage of being soluble in Alcohol of 65%. *See also table antea.* Sesquiterpeneless Lemon Oils are, however, made of different solubilities and concentrations for customers' particular requirements, and the preparation varies accordingly. The Terpeneless Lemon Oil is dissolved in Spirit and the required quantity of Sesquiterpene is thrown out by the addition of water. The Alcoholic fraction is drawn off and the Alcohol and water removed in a vacuum when a Sesquiterpeneless Lemon Oil will be obtained soluble in Alcohol of the strength required. This process is attended with technical difficulties, as the separation of the two layers is anything but accurate.

As regards **adulteration of the Natural, Terpeneless, and Sesquiterpeneless Lemon Oil**, there is little to be said. It is impossible to state to what extent adulteration is now taking place as the only two adulterants used are Lemon Terpene obtained from the manufacture of Terpeneless Lemon Oil, and an extremely highly purified Citral obtained from Lemongrass Oil. Both these products are to be found in natural Lemon Oil and hence it is only by the aroma and flavour of the oils that adulteration can be discovered. In several instances, it is not even possible to discover adulteration of Terpeneless Lemon Oil with Lemongrass Citral either by aroma or flavour. Examples of adulteration of these three oils with the old adulterants are rare; in fact it may be safely said that no adulterants are now used, other than those mentioned above.—W. C. Slater, 1925.

'**Oleum Citron**' so called, in this country is usually a blend of Lemon, Orange, etc. (Distinguish from *Oleum Citri*—"Citronenöl" P.G. VI. which is our *Oleum Limonis*—*vide antea*). **Bergamot Oil** is from *Citrus bergamia* peel, by expression from the ordinary Bergamot. Sp. Gr. 0·882 to 0·883.

OLEUM MENTHÆ PIPERITÆ (B.P. '14).

Peppermint grown in a damp situation is said to yield only ½ the amount of oil of that grown under ordinary conditions, but this is not the case in experiments at Hitchin. Cultivation in the shade does not appear to increase yield of oil.

About 7 to 10 lbs. of oil obtained from 1½ tons of fresh peppermint.—P.J. ii./22,317.

B.P. '14 requires Sp. Gr. 0·900 to 0·920, O.R. -20° to -35°: not less than 50% Menthol and not less than 5% Esters calculated as Menthyl Acetate.

Menthol and Peppermint Oil in Alcohol Solution.—Test to distinguish.

If Tincture of Iodine be added to a Solution of Peppermint Oil, several drops, more or less, may be added before the yellow tint of Iodine is perceptible. With a solution of Menthol there is no absorption, so the yellow tint is seen at once.

Piedmontese Oil—The district said to be the Mitcham of Italy. Mitcham plants introduced paid for cultivation.—C.D., 1920, 1507.

The content of free Menthol in Peppermint Oil produced in MANCHURIA, from plants taken from Japan, gradually decreases with increasing lapse from the time of transplantation. Some of the Menthol appears to be converted into esters, and Menthone and Limonene were detected.—P.R.'Jan.'24,14.

A Peppermint Oil from WESTERN AUSTRALIA compared favourably with the best American production and nearly resembled English distilled Oil.—E. J. Parry, P.R.'24,188.

A German patent (1921) describes a process for converting **Oil of Pennyroyal** into an oil resembling Peppermint Oil and containing a high content of Menthol, by reducing an ethereal solution below 5°C. with Sodium and Water. This process applied to Pulegone gives a product with all the properties of Menthol. Previous observers (1891), by reduction in Anhydrous Ether, obtained large amounts of d-Menthol instead of the naturally occurring lævo isomer.—P.R.'24,55.

Menthol from Mexico.

The Department of Industry, Commerce and Labour, in Mexico, advises the exploitation of a plant known as *tabaquillo*, but botanically termed *Hedeoma piperita*, Benth., which grows wild in Mexico in large quantities. The use of the name *tabaquillo* may prove misleading, as there are no less than six plants to which the name is applied in Mexico.

Further investigation of the two plants *Calamintha macrostema*, Benth., and *Hedeoma piperita*, Berthé, both known as *tabaquillo*, is desirable; although both may contain menthol, the other constituents of the volatile oil present in each may be different.—E. M. Holmes, C.D., Nov. 24/28.

OLEUM MORRHUÆ (B.P. '14).

(See also Vol. I., p. 616.)

NOTE.—The chapters on *Nutriments* (*Accessory Food Factors—Fat Soluble A'*) both in Vol. I and this volume should be consulted for Vitamin Information.

The 5th Report of the **Imperial Economic Committee on Marketing and preparing for Market of Foodstuffs Produced within the Empire** states that for relative richness in Vitamins **Scottish Oils rank first, then Newfoundland, then Norwegian**, but the last is usually the best from the marketable quality of colour and odour. Newfoundland oils do not find a ready sale in Gt. Britain—the price is often high. In Gt. Britain the market value of Cod Liver Oil depends less on its true medicinal value than on its acceptability by the public.—C.D. ii./27,357.

Norwegian Cod Liver Oil Industry. Bergen is the centre of the industry. Yield of oil in 1928 (a poor year) was 50,000 hectolitres, against 70,000 in 1927. In marketing, some of the dealers fill the air space above the oil with CO₂ and Nitrogen to prevent oxidation.

J. W. England points out that the total activity of Cod Liver Oil does not reside in its Vitamin 'D,' or in 'A' + 'D,' any more than Quinine represents the total activity of Cinchona Bark. He draws attention to the *Phosphatides*, and the high content of *unsaturated fatty acids*, *vide infra*.—Joseph W. England, Jl. Am. Pharm. Assn., Feb., '29. For a further reference to this paper, see *Vitamin Chapter*.

Sp. Gr. 0.924—0.931 includes all genuine samples. **Unsaponifiable Matter.** In good quality oil rarely exceeds 1.6%; use full excess of alkali before extraction; wash Ethereal Extract at least 4 times (Parry). **Free Fatty Acid** calculated as Oleic should not exceed 1%, easily estimated.

Many samples fall below 0.5%. **Iodine Number** 155 to 170 (Hübl's Solution ditto). We found Acid Value not exceeding 2.5. No separation of solid fat should take place on exposure of the oil to a temperature of 0° C. for three hours. (*B.P.* '14). 1 Cc. of the oil dissolved in 10 Cc. of Carbon Disulphide may give a violet blue colouration when gently shaken with one drop of Sulphuric Acid.

Over 50% of the medicinal oils give Refractive Index 1.4801 to 1.4802. The Iodine value in Best Medicinal Oils was 151.1 to 178.7.—Evans.

Unsaturated Fatty Acids in the Oil.

Cod Liver Oil is composed almost entirely of unsaturated fats. An increase in the amount of unsaturated fatty acids in the environment of the tubercle bacillus tends to disintegrate it. An increase of unsaturated fatty foods yields an increase of the same in the blood, and the bacillus is present in the blood in comparatively early cases of phthisis. Increase of saturated fat above a certain point retards its absorption from the intestine. The saturated fat is assimilated up to about 14% only; unsaturated, on the other hand to extent of 98%. In mixed diet the unsaturated help the saturated to become absorbed. The highly **Unsaturated Acids** contained serve the immediate needs of energy production and the *saturated* are stored in the nature of a reserve.

It may be well to remind non-chemical readers that the saturated fatty acids are those in which all the valencies of the Carbon atom are fully satisfied, as, for example, in Acetic Acid—the first of the series containing Palmitic and Stearic Acids. The **Unsaturated Acids** have some of the Carbon Valencies unattached to other elements and hence have double bonds, thus $C=C$, e.g., Acrylic Acid—the first of the series containing **Oleic Acid**.

Cod Liver Oil should be prepared **under conditions preventing oxidation**, both from the aspect of this theory and the newer Vitamin views.

Cod Liver Oil is a food—it enters into permanent combination with a body cell yielding energy to it and altering the whole of the cell's relations by becoming an integral part of the cell protoplasm. It is more readily absorbed than other fats and has probably a marked action on metabolism.

The greater part of the fat obtained from animal tissues is not real fat, but to a great extent complex combinations of fatty acids with Glycerophosphoric Acid and Nitrogen-containing compounds—the so-called **Phosphatides**—this is the portion actually made use of by living cells. Phthisical patients treated with Cod Liver Oil have been observed and effects on *Nitrogen metabolism* found to be marked and the beneficial effect on *fat absorption* was also considerable.—O. T. Williams.

Cod Liver Oil is normally digested and absorbed before it reaches the lower bowel, hence it is not a laxative.—E. Pritchard, *B.M.J.* i./15,489.

Bases to the extent of 0.05% have been found, including Butylamine, Isoamylamine, Hexylamine, Dihydrolutidine, which are volatile and the non-volatile Morrhaine $C_{13}H_{27}N_3$ and Aselline $C_{25}H_{52}N_4$. Fahrion assumed the presence of Ascllic Acid $C_{17}H_{32}O_2$ in the liquid fatty acids from Cod Liver Oil, which had I.V. 175.5. Cholesterol is a characteristic constituent ranging from 0.46 to 1.3%.—Benedict and Lewkowitsch.

Phosphorus, it is said, is not found in neutral oils, but only in acid samples and Iodine only when decomposition of the liver has occurred. The activity of the oil is not due to these bodies. Presence of the last mentioned may be sought by fusing with Sodium Carbonate

I.V.'s (by Wij's method) 118.4—178.7 were found for the oil and 165.6—178.7 for the Acids obtained therefrom, indicating molecular values 319.7—524.4. Hydroxylation and polymerisation between the double bonds and Carboxyl groups may possibly account for a decrease in I.V. In an attempt to prepare the Acids as they exist in the oil, e.g., by treating with Alcoholic Potash in presence of Hydrogen, an acid with 18 carbons and 4 double bonds having a molecular weight of 290.5 was obtained.—Owen T. Williams, *P.J.* ii./12,806.

E. F. Harrison regarded Iodine Monobromide as the most trustworthy reagent. He obtained I.V. 165—170 for the Oil. O. T. Williams stated he had subsequently obtained similar figures on other samples of oil, cf., Vol. II p. 619.

OLEUM OLIVÆ (B.P. '14).

Sp. Gr. 0.915 to 0.918. U.S.X. Saponification No. is 190 to 195 and Iodine No. not less than 79 or more than 90. *B.P. '14* differs slightly in Iodine No.

The production of olive oil has made great strides in California and South Australia. The colour of the oil varies considerably from water-white to golden-yellow. Low-class oils have a green tinge. It should taste pleasant and soft, but the taste varies according to the locality, etc. Thus oils from Tuscan olives are more palatable than those from Ligurian olives. An oil may be quite pure and unadulterated but be inferior on this point. The large quantity of edible oils produced in Tunis are frequently admixed with the best brands of French and Italian edible oils to cover the harsh flavour.

Excluding abnormal oils, a high iodine absorption may indicate adulteration with as little as 5% of a drying oil or 15% of sesame, cottonseed, and rape oils. The saponification value will only lead to definite results if large quantities of rape oil have been added. In the claudin test, olive oil yields of all oils the hardest elaidin, and also solidifies most quickly, but this test can only be used as a preliminary. The examination of unsaponifiable matter is necessary if the addition of lard is suspected. Green olive oils should be tested for copper. C.D., Commercial Compendium, Apl. 7/28, *q.v.* for further data.

Halphen's Test for Cotton Seed Oil.—2 Cc. of the Oil mixed with 1 Cc. of Amyl Alcohol and 1 Cc. of a 1% Solution of Sulphur in Carbon Disulphide and placed in a test tube immersed in boiling water or boiling brine should not develop a red colour in 15 minutes—absence of.

For Arachis Oil.—Boil 1 Cc. of the Oil and 15 Cc. of Alcoholic N/1 KOH for 20 minutes under reflux condenser and keep 24 hours at not exceeding 15° C. A cloudiness or distinct deposit of crystals (Potassium Arachidate) would indicate presence of Arachis Oil.

For Sesame Oil.—2 Cc. of the Oil shaken for $\frac{1}{2}$ minute with 1 Cc. of strong Hydrochloric Acid containing 1% of Cane Sugar and allowed to stand for 5 minutes, the acid layer should not become pink (U.S. slightly modified). Our experiments showed that 5% or even less of Sesame Oil working with a pure control is quite easily detected by this test. We found that 20% of Sesame Oil gives a deep red. The reagent must be freshly prepared.

It is also necessary that the Sesame Oil shall be recent. We have found that old Sesame Oil fails to give the red colour—on the contrary, it produces a characteristic light green colour.

Olive Oils ought not to be condemned as impure on the basis of the test. Experiments with Spanish, Italian, etc. brands.—C. E. Sage, P.J. i./15, 128.

Modified B.P. Test. Dissolve Cane Sugar 0.1 Gm. in 5 Cc. Hydrochloric Acid and allow to stand 15 to 20 minutes at 20 to 25°C. The colour will then be faint cream. Shake 5 Cc. of the solution with 10 Cc. of the oil and 5 Cc. of Petroleum Spirit for 10 minutes. By this means $2\frac{1}{2}$ % of Sesame Oil can be detected. The B.P. method may miss more than $2\frac{1}{2}$ %.—Evans.

Nitric Acid Test for other Oils.—Agitate 5 Cc. of the oil with 5 Cc. of HNO₃, Sp. Gr. 1.30 and heat for 5 minutes. There should be no darkening and the oil should have set firm in 12 to 18 hours.

For Tea Seed Oil. (Bieber's Reagent).—It is impossible either by chemical or physical constants or by available colour tests to ascertain whether Olive Oil is adulterated with Tea Seed Oil.—H. A. Caulkin, B.P. Conf., 1927, per P.J. i./27, 770; See also J. Cofman Nicoresti, P.J. i./20, 139.

Prepare a mixture of concentrated nitric acid, concentrated sulphuric acid and water, equal parts by weight. Of this mixture 10 Cc. is well shaken in a test-tube with 10 Cc. of the oil to be analysed, and placed in boiling water for twenty minutes. Should any tea-seed oil be present the oil layer changes to a cherry-red colour. The colour varies with the amount and quality of tea-seed oil present, the crude oil gives a deeper colour. When cool, samples of pure olive oil solidify to a yellow, nearly white, mass, while the adulterated oil remains liquid or semi-solid, according to the amount of tea-seed oil present, having the characteristic colour. When the tea-seed oil is less than 20 per cent. it is better to work on 50 Cc. of oil and 30 Cc. of the acid mixture.

Our experiments with the test gave the following:—

1. **Tea Seed Oil** 10 Cc. and 10 Cc. of the mixed acids, the oily layer quickly turned dark brown, nearly black. On continued heating as directed the

colour fades partly, leaving an orange red coloured layer, containing black particles in suspension. On cooling, the oily layer becomes very thick, but gives no signs of solidifying.

2. **Olive Oil and Tea Seed Oil** mixed in equal parts, on heating with the acid mixture became light brown, and on continued heating faded to a dark yellow tint. On cooling the oily layer became semi-solid.

3. **Olive Oil** used alone, the change in colour is very slight, and at the end of twenty minutes' heating had only assumed a lemon yellow colour. On cooling the oil settled to a solid mass.

4. **Nut Oil.** In this case the colour change is more marked than with Olive Oil. After 20 minutes' heating the oil had assumed an orange colour. This on cooling solidified in an exactly similar manner to Olive Oil, the only difference being the slight darkening in colour.

Modification of the Nitrous Vapour Test found to show 5 to 12% or more of Tea Seed Oil.—H. Blin, Y.B.P., '22,96.

A sample of Olive Oil was found to be extremely bitter, a colour with Baudouin's Test being the only other abnormality. It seems probable that this was due to the presence of Oleoeuropein, owing to unfavourable climatic conditions in Spain. This glucoside is normally hydrolysed by Emulsin before the fruit is pressed, but its presence in some stage of hydrolysis may account for the fact that some oils, without being bitter, may give a positive Baudouin's Test.—F. F. Shelley, P.R., '24,274.

Olive Oil obtained by **solvents from the press cake** can be identified, even in small amount. Heat about 2 Cc. with an equal volume of Acetic Anhydride, shake, cool, and filter. In a dish add a few drops of Conc. Sulphuric Acid to the filtrate. A cherry red colour, which, on adding water, turns green gradually disappearing shows an extracted oil.—Analyst, '26,416.

OLEUM ROSMARINI (B.P. '14).

A colourless or pale yellow oil soluble 1 in 1 of 90% Alcohol and 1 in 5 to 10 of 80% Alcohol. Distilled from flowering tops of *Rosmarinus Officinalis* (Labiatae). Sp. Gr. from about 0.895 to 0.920. U.S.X. requires not less than 2.5% Ester calculated as Bornyl Acetate and not less than 10% of total Borneol.—B.P. '14 requires practically all these constants.

Cineol Estimation by Cresineol Method. See *Oleum Lavandulae*.

SICILIAN OIL gave Sp. Gr. 0.918 to 0.921, O.R. + 9 to + 5.6°, R.I. 1.466 to 1.4659, Esters 3.75 to 5.25%, Free Alcohols 6.44 to 8.64%, Total Alcohols 9.33 to 12.77%. The first figures in each instance were from plants gathered in August, the second February and March.—G. Pellini, C. D., Sept. 15/23.

Internally it is a carminative, and externally promotes the growth of the hair.

OLEUM SANTALI (B.P. '14).

Sandal Wood Oil should be soluble 1 in 6 of 70% alcohol at 20° C. It should contain not less than 90% alcohols, calculated as santalol, $C_{15}H_{24}O$.—Sp. Gr. 0.973 to 0.985.

O.R. (B.P. '14).—13° to —21°. Refractive Index 1.498 to 1.508 at 25° C. U.S. Specification is similar. The Oil is distilled in Government factories in Mysore.

West Australian Sandalwood Oil of good quality is now available, containing 95% Alcohol (calculated as Santalol) and closely resembling the East Indian oil, although it has not been proved that the Alcohols are identical with the Santalols of the East Indian oil. The oil, which is obtained from *S. Spicatum* and *S. lanceolatum*, is not inferior therapeutically to that obtained from the *S. Album*.—P. May, P.J. i./28,368.

No evidence that the Alcohols in W. Australian Oil differ from those of Mysore Oil, and its therapeutic value is at least equal to that of *S. Album*.—W. H. Simmons, C.D. i./28,171. See also a *contra* view.—A. R. Penfold, C.D. ii./28,496. Earlier refs. in 18th Edn.

Copaiba.

B.P. '14 has Sp. Gr. 0.975 to 0.995.
 For Maranham and Maracaibo varieties the Acid Number is at least 75. Para and Bahia varieties contain a greater proportion of volatile oil, consequently lower acid number.—Umney.
P.G.V. had Acid No. 75.8 to 84.2, Saponification No. 84.2 to 92.7. These are not given in *P.G. VI.*
Test for Gurjun Balsam (U.S.X.).—One drop of Nitric Acid is mixed with 3 Cc. of Glacial Acetic Acid and four drops of the oil separated from the sample by distillation with steam are added. No red zone appears, nor does the liquid become red or purple on shaking.
 Loses 45% of its weight when heated at 100° C. for 48 hours.—*B.P.* '14.
 When heated on the water bath a hard and brittle resin remains weighing not less than 36% of the original weight taken.—*U.S.* (Paraffin or fatty oils).
 For further details of Copaiba see *Oleum Santali, Vol. I.*

OPIUM.

A poppy grown in this country does not elaborate Morphine in the latex.—*W. E. Dixon, C.D. i./28,747. We confirmed that this is apparently the case by examining capsules of our own growing (1929).*

Indian and other Governments have reason to regard Opium as as much a necessity for the natives in many parts as is Quinine for the inhabitants of malarial districts.—*P.J. ii./24,332.*

Addiction to Opium, Morphine, Cocaine, etc., in this Vol. is dealt with, so far as recent notes go, under Cocaine. See also individual chapters Vol. I.

The ash of opium should not exceed 4% to 8%, moisture about 12%.

In the official assay process the Chlorine of the Ammonium Chloride combines with the Calcium and, the Calcium Morphinate being decomposed, the Morphine is precipitated in the Saline solution in which it is sparingly soluble.—*D. B. Dott, P.J. ii./18,318.*

Of the 20 or more alkaloids in Opium, six are of more importance than the others. These occur in Turkey Opium as follows, approximately:—Morphine 9, Narcotine 5, Papaverine, 0.8, Thebaine 0.4, Codeine, 0.3, Narceine 0.2.—*P.J. i./12,161.*

Extraction of Opium Alkaloids.

The plant is extracted with warm water and an equal volume of Alcohol and excess Ammonia is added, precipitating Morphine and Narcotine, the latter being separated by treatment with Benzene or Chloroform, in which Morphine is insoluble. The mother-liquors are treated with dilute Acetic Acid, and from this Papaverine can be extracted with Benzene. The strong bases, Codeine and Thebaine, forming salts, remain in solution, and can be separated by the addition of alkali which precipitates Thebaine, Codeine remaining in solution.—*J.C.S., A. i./25,153.*

Estimation of Narcotine and Codeine in Opium.—*Y.B.P., 1903,122.*

Assay from International standpoint.—*D. B. Dott, P.J. ii./20,199; Y.B.P. 1920, p. 18; see also P.J. ii./20,302; Y.B.P., 1920,23.*

Indian Opium, contrary to statements in *Allen's Commercial Organic Analysis*, found to contain as average during 7 years not less than 7% of Morphine.—*J. N. Rakshit, Analyst, 1921,46,481. Y.B.P., 1922,16.*

Modified Dowdard Process for Assay of Opium Tincture.

Evaporate 100 Cc. to 25 Gm. on water bath. Mix intimately on cooling 3 Gm. Calcium Hydrate with a small pestle. Transfer to flask graduated at 102 Cc. Shake well seven or eight times in the half hour's digestion. Filter off and pipette 50 Cc. to an oval flask with 30 Cc. Ether, 5 Cc. Alcohol 90%, and 2 Gm. Ammonium Chloride. Shake 30 minutes, stand over night, remove Ether layer with a straight pipette through inter-leaved filter papers, shake residue with 15 Cc. Ether. Again pipette off and wash papers with 5 Cc. Ether (0.720) twice, thoroughly evaporate Ether from the papers and then filter aqueous residue (Morphine finally), washing pipette, etc., with 100 Cc. Morphinated water. Dry filter papers by identical compression. Digest each with 20 Cc. N/10 Sulphuric Acid, pulp the papers thoroughly, dilute with water and back-titrate with N/20 Sodium Hydrate using Methyl Orange.—*H. R. Jensen, P.J. ii./13,876.*

The presence of Milk Sugar, *i.e.*, as diluent of Opium, may interfere markedly in the U.S. assay process. Milk Sugar is no longer specified as a suitable diluent in U.S. Starch also interferes.—P.J. ii./13,647.

In powdered Opium the amount of Morphine compounds insoluble in water appears to increase with age of the sample. Amount of total Morphine is also reduced.—P.J. ii./12,781.

By **drying the Opium** and passing through a No. 20 sieve it is possible to extract it perfectly when making tincture by maceration and percolation with 45% spirit at least as completely as can be done in the B.P. process of analysis. The waxes, etc., present in Opium certainly affect the extraction of the alkaloids. B.P. process is wasteful and troublesome. Redwood's process of 1885 should be reverted to with addition of percolation. Opium in powder loses strength but liquid preparations do not.—A. C. Abraham, H. E. Digby & J. Rae, P.J. i./22, 353.

Brom-phenol-blue recommended as indicator for titration of Morphine. A 1% solution of Morphine Hydrochloride has a pH of 3.65.—N. Evers, B.P. Conf., 1921; P.J. i./21,470.

Morphine and other alkaloids in animal excreta. Detection in organs, urine, etc.—Y.B.P., 1922,12.

The fate of Morphine in the animal body, with a method of estimation in body fluids and tissues.—Jl. Ph. & Exp. Ther., June, '27,177.

Standardisation of all the Active Constituents of Opium suggested, *i.e.*, Morphine, Narcotine, Codeine and Meconic Acid, not on Morphine content alone.

The estimation of Meconic acid is colorimetric by means of (1) precipitation with Goulard's Extract; (2) subsequent comparison of the colour produced with Ferric Chloride—using a control of pure Meconic Acid. The paper should be consulted.

As a result of the examination of four samples of Opium the author found:—

Morphine	12.2%	14.1%	10.5%	12.4%
Narcotine.. . .	5.8%	4.8%	6.8%	7.6%
Codeine	1.1%	0.7%	1.5%	0.9%
Meconic Acid . .	5.4%	4.3%	4.5%	6.4%

—P. Van der Wielen, P.J. ii./13,114.

Estimation of Morphine in Omnopon and other Opiates.

Liberate the alkaloids by Sodium Bicarbonate and extract those other than Morphine by Chloroform saturated with Morphine; the Morphine is then extracted by a mixture of equal volumes of Isobutyl Alcohol and Chloroform, the extract is shaken with a known amount of standard Hydrochloric Acid, the excess of which is found by titration. Results are about 1.5% to 0.3% high.—E. Anneler (Arch. Pharm., 1912,250, 186-198). J.C.S.A. ii./12,8199.

Ammonia is present in Opium to the extent of 0.2 to 0.3%. The odour of Ammonia is noticeable in estimating the Morphine content in Opium on liberating the alkaloids with lime in the B.P. process.—J. N. Rakshit, P.J. i./17,255.

Estimation in Acid Liquids, *e.g.*, **Sydenham's Laudanum** of the Codex.—P. J. ii /13,881.

Assay of Acetum Opii, N.F. (Formerly U.S.). Owing to the amount of Acetic Acid and the large amount of Acid, the ordinary lime method is not suitable. It is best to proceed thus: Mix 40 Cc. with the calculated quantity of lime, to nearly neutralise, evaporate to a syrup, and extract with successive quantities of Spirit. Evaporate the alc. solution to near dryness and make up to 41 Cc. with lime and water. Collect the Ammonium Chloride precipitated from 25 Cc. of filtrate, solve in boiling Spirit, filter the solution through the same filter, and wash the latter with hot Spirit and titrate. The % indicated was 0.86w/v.—D. B. Dott, P.J. ii./24,688.

Loss in morphine content of powdered Opium on storage.—H. E. Annett, P.J. ii./22,304. See also C. F. Sage, *ibid* 353; P. A. W. Self, *ibid* 373.

A mixture of the alkaloidal hydrochlorides may be shaken with a buffer solution of pH 8.6 and Ether. Morphine is separated and can be dissolved in acid and the excess titrated. The aqueous filtrate is treated with Sodium Hydroxide and shaken out with Ether. The Ethereal solutions are combined, evaporated, dried, and weighed for the determination of the remaining alkaloids.—P.J. i./25,638.

Morphine Estimation in Poppy Extracts. Alcohol 90% was found to extract the alkaloid, the extracts being naturally acid in reaction. Isopropyl Alcohol gave identical results.—C. T. Bennett and D. C. Garratt, B.P.C., 1926, C.D. ii./26,235.

Determination of Morphine using Barium Hydroxide.—B.C.A., '28, A1145.

Morphina.

For details of efforts at Synthesis of derivatives of Morphine (the structure of which is not known with certainty) *vide*—May.

Solubility in Carbon Tetrachloride is 0.0156 Gm. in 100 Gm. at 18 to 22° C.

Spectrum lines characteristic for Morphine are obtainable with 1/200 grain.—J. J. Dobbie, L. i./13,1399.

Morphine Colour Test.—On dissolving 0.01 Gm. of morphine hydrochloride in 2 Cc. of sulphuric acid and carefully layering on a solution of hydrogen peroxide (3%), at the junction of the two liquids a yellowish brown coloration develops in the upper layer, and a bright emerald coloured ring in the lower layer. Methyl-morphine hydrochloride, ethyl-morphine and apomorphine also yield the coloration which, however, is not produced by other opium alkaloids.—L. Ekkert, C.D., June 23/28,777. *We found the test satisfactory as stated.* Papaverine gives a red color.

Gregory's Salt. An impure Morphine Hydrochloride, being a mixture or double salt of Morphine Hydrochloride and Codeine Hydrochloride occurring in the manufacture of Morphine.

Codeine, in various Indian Opiums, 0.6 to 1.84%. Method of proceeding.—J. N. Rakshit, Analyst, 1921, 46,481, Y.B.P., 1922,16.

Ethyl Morphine Sulphate ($C_{17}H_{18}O_2NO_2C_2H_5)_2H_2SO_4 \cdot 5H_2O$ is soluble 1 in $9\frac{1}{2}$ of water at 15.5° C. and 1 in 111 of Alcohol 90%.—J. L. Thomson, P.J. i./20,7.

Diamorphine Hydrochloride. FR. CX. SUPP. II. TEST.—Place 0.05 Gm. in a porcelain capsule. Add 2 drops HNO_3 (63.64%). A yellow coloured solution results. Heat gently over a small flame until the liquid begins to assume green colour. Remove from heat. The liquid will gradually assume a deeper colour. Morphine, Ethyl Morphine and Codeine do not yield this.

Morphine, Hydrogenation of, by using Platinum or Nickel Oxide catalyst.—J.C.S.I., 1921, 40,446R, Y.B.P., 1922,1. *cf.* Colchicine and Quinine Hydrogenation.

Cryptopine, Gnoscopine, Meconine, Papaverine, and Xanthalline—are other constituents of opium. Papaverine has recently attracted attention therapeutically.—See Vol. I.

Laudanosine (another body).—Yields on oxidation *Lodal *vide* Edn. XVII, Vol. I, p. 549.

Cryptopine—W. H. Perkin, Trans. Chem. Soc. 1916, p. 815 (B.M.J. i./17, 836) worked on this alkaloid, to produce 5 ozs. of which 10,000 lbs. of Opium were needed. Oxidation experiments show the probable molecular arrangement of it and protopine and allied bodies.

Hydroxycodine. *Syn.* Neopine. A new amorphous alkaloid found by T. and H. Smith in small quantity in the last Opium Alkaloid Mother liquors. Readily soluble in water, Alcohol, Ether and Chloroform. Hydrobromide and Hydrochloride both crystallise well.—J.C. S.T., '11,34.

All the Acyl compounds of Morphine, *e.g.*, **Diacetylmorphine** and **Benzoylmorphine**, are readily decomposed and Morphine recovered from them, whereas the Alkyl derivatives, such as **Codeine** and **Benzylmorphine**, are intimate compounds from which the Morphine cannot be recovered. The former are strong narcotics like Morphine, and the latter only weak narcotics.—D. B. Dott, P.J. ii./28,250.

Apomorphinae Hydrochloridum.

The correct formula is no doubt $(C_{17}H_{17}NO_2HCl)_4 \cdot 3H_2O$. It is customary to give formulæ of alkaloidal salts with their full water of crystallisation, though books commonly describe the anhydrous salt.—D. B. Dott, P.J. ii./21, 102. For further details of Dott's previous work on the subject see Edn. XVII., Vol. II., p. 124,125.

It is a very hygroscopic salt. We found that on drying a sample of commerce and then placing over Calcium Chloride it reverted to the content of water originally present, viz., 3.4%.

Sufficient Apomorphine to produce vomiting can be absorbed from the environment of the eye, even when the tear ducts are not patent; absorption of poisons from the external ear cavity is also possible.—Macht, J.A.M.A., Dec. 8/23, P.J. i./24,14.

OXYGEN.

Atmospheric Pollution.

The percentage of CO₂ in crowded rooms has nothing to do with the sense of discomfort. It cannot get into the body—respiration prevents it. The amount of this gas in the lungs is always kept the same. A person placed in any CO₂ containing atmosphere will not feel ill effects until the amount rises to over 60%—the normal amount in the lungs. Similarly the oxygen in a crowded room is never diminished by more than 1%—this diminution has no physiological effect. The real source of pollution and infection is in the speaking, coughing and sneezing by man—the spray of saliva passing out from the mouth. Pneumococcic and other cold infection from man to man in this way has been conclusively proved.

L. Hill and F. F. Muecke investigated the reason why people (children) exposed to the weather and wind never catch colds, whilst the moment they return to crowded places and chill autumn weather and they return to schools the colds run round and everyone catches them. The reason is to be sought in the fact that the mucous membrane in the cool surroundings and outside air is taut—there is very scanty secretion, whilst a heated room pretty well saturated with moisture causes the mucous membrane of the nose to become turgid with blood and covered with thick secretion and the tissues are all swollen. (A fan in a hot room causes the opposite effect—bringing the membranes into the first state again.) On going out into the cold open air the blood goes out as the vessels contract, but the mucous membrane is still boggy, its pits and the secretion (and tissue lymph) is thick upon it—a medium for the growth of bacteria. Adequate ventilation is essential. The immunity to 'colds' of those who live an open air life is well known. Keep the air in rooms cool and in motion. Confinement of air space, radiator heating, absence of movement of the air (draughts) in modern buildings and the like is diminishing metabolism and vigour, health and happiness—quite apart from causing consumption. Skyscrapers and the artificially lighted cellars people have to live and work in must be condemned.—Leonard Hill, L. i./13,1286 *et seq.*, see also L. ii./12,767.

Oxygen Content of the Air.—212 determinations during period of ten months April, 1911—January, 1912, showed no material fluctuation despite all possible alterations in climatic conditions, including periods before, during and after the vegetative season. The averages were 20.952% Oxygen and 0.031% Carbon Dioxide which maintain the results of Cavendish in 1783 and de Marli in 1787 as to the uniformity of air as regards its Oxygen content.

The interdependence between the amounts of Oxygen and Carbon Dioxide is so constant that estimations of the latter made in the Loudin apparatus may be taken as accurate indications of the Oxygen content, *e.g.*, for every 0.01% increase in Carbon Dioxide a corresponding increase in the percentage of Oxygen may be assumed.—Na., June 19, 1913,400.

The Atmosphere of London Underground Railways.

The ratio of the number of organisms which develop at room temperatures (about 20°) is about 14 for railway air to 10 for outside air, but for organisms developing at body temperature the ratio is 2 to 1, the mean number per litre for railway air being 9 and 4.6 respectively. While some of the organisms met with occur in mouth, nose, and on surface of body, in no instance were pathogenic organisms present, other than certain moulds, *e.g.* *Aspergillus niger* and *A. fumigatus*.—Na., 113. '24,691.

The 13th Report of the Advisory Committee on Atmospheric Pollution suggests the possibility of setting up limits or standards of permissible pollution. There is a tendency towards improvement, but this is chiefly in the moderately clean cities—the very dirty cities show little change.—L. ii./28,563.

Mechanism of Infection.—Oxygen inhalation in general infections should be employed as an antiseptic agent, increasing the power to destroy disease organisms.—W. R. Meadows, P.J. ii./28,576.

Air Liquefying Apparatus (Hampson's Patent).

This apparatus depends upon a method by which a moderate amount of refrigeration, produced by the expansion of a gas, may be accumulated and intensified till it reaches the point at which the gas becomes liquid under atmospheric pressure. The method consists in directing all the expanded gas immediately after its expansion, over the coils which contain the compressed gas that is on its way to the expansion point. The cold developed by expansion in the first expanded gas is thus communicated to the on-coming compressed gas, which consequently expands from, and therefore to, a lower temperature than the preceding portion. It communicates in the same way its own intensified cold to the succeeding portion of compressed gas, which in its turn is made colder both before and after expansion than any that had gone before. This intensification of cooling goes on until the expansion temperature is far lower than it was at starting, and the effect is so powerful that even the small amount of cooling due to the free expansion of gas through a throttle-valve may be made to liquefy air without using other refrigerants.

The amount of refrigeration due to free expansion was ascertained by Joule and Thomson, and is in the first place proportional to the fall of pressure. Air at 0° C. is cooled 0.29 of a degree C. for every atmosphere of pressure-drop. This cooling, however, increases with the descent of the temperature from which expansion takes place, and the law is that it is inversely proportional to the square of the absolute temperature. Thus expansion of air from $4\frac{1}{2}$ atmospheres to 1, and from a temperature of 0° C., i.e., 274° Absolute, gives about 1° of cooling in the air itself. But when the air expands from $\frac{2}{3}$ of that absolute temperature, i.e., from 91° absolute, the cooling for the same pressure drop is $\frac{2}{3}$ of 1° , or $2\frac{1}{3}^{\circ}$.

In the liquid state air occupies $\frac{1}{800}$ th part of its ordinary volume, or in other words if liquid air be vaporised and restored to normal temperature it will expand 800 times.

Oxygen can be obtained from Liquid Air up to 80%.—B.M.J. ii./19,77.

Vacuum Vessels (Thermo-Isolators).

Are necessary for the storage of liquid air and those gases which only liquefy at low temperatures.

They are either cylindrical or globular, and consist of one glass vessel enclosed within another. The space between these vessels is thoroughly exhausted and sealed under a high permanent vacuum. Heat radiates across the vacuous space very slowly, consequently liquid stored in a vacuum vessel is admirably insulated from the action of external heat and only vaporises slowly.

The efficiency of the vacuum vessel is increased by silvering as radiation from outside is thus partially reflected.

Liquid air evaporates from vacuum vessels at the rate of from 5% to 15% per 24 hours, according to the size of the vessel, the evaporation from small vessels being more rapid than from large.

* **Thermos** (T.M. No. 296745, Class 13 and 289470 Class 15) Flasks are on the principle of vacuum vessels.

Hydrogen Liquefying Apparatus (Morris W. Travers').

It has been found that hydrogen, when compressed at normal temperatures and allowed to expand in an apparatus like the Hampson Air Liquefier, does not become cooled but on the contrary slightly heated. When, however, its temperature is reduced to -80° C., or lower, before it enters the regenerator coil, it becomes further cooled on free expansion, so that the principle of self-intensive cooling employed in Hampson's Air Liquefier can then be applied to the liquefaction of this gas.

(For further information on liquefaction of gases, see "The Experimental Study of Gases," by Prof. Morris W. Travers.)

Hydrogenit is said to be a mixture of dry Soda-lime and ferro-silicon or other silicon alloy. When acted upon by heat 3 kilos give about 1 cubic metre of hydrogen.—Chem. Zeit., 1911, 35, 1, 273, per P.J. i./12, 31.

The preparation and commercial uses of hydrogen.—A. W. Crossley, P.J. i./14, 604, 637, 676.

Calcium Hydride or **Hydrolete** CaH_2 , is used as Hydrogen generator by decomposing with water.

Ferrosilicon process. Ferrosilicon falls into Sodium Hydrate solution (covered with Hydrocarbon Oil to prevent frothing). Also other processes. Silicon alone is also used.—P.J. II./15,214.

Water Gas may be converted into **Hydrogen** and CO_2 by passing it over Iron Oxide, the reduced Iron being regenerated by steam. The more modern way is to 'purify' water gas by mixing it with steam and passing it over a catalyst ($\text{H}_2\text{O} + \text{CO} + \text{H}_2 \rightleftharpoons \text{CO}_2 + 2\text{H}_2$). The CO_2 is absorbed by passing the gases through water under pressure.—C.D. Compendium.

PANCREAS.

Pancreatinum.

THE EFFECT OF

CERTAIN CHEMICALS AND DRUGS ON THE ACTION OF PANCREATIN.

As supplementary to our work on Pepsin, we conducted experiments to determine which chemicals and "drugs" in a selected list prevent the proteolytic action of Pancreatin with certain conditions.

The substances chosen were almost identical with those in the Pepsin experiments (*vide postea*). In the Pancreatin series, however, we omitted the acids, as these are generally held to be incompatible. W. M. Bayliss ('Nature of Enzyme Action') says Trypsin is practically inert in acid or neutral solution. Chittenden and Cummins, however, state (O. Hammarsten) that when the acid is combined with protein bodies digestion may take place rapidly when the acid combination is not in too great excess.

One quarter average doses of the substances were mixed with 150 Cc. of a 3.5% Casein Solution prepared by aid of 0.35% Sodium Bicarbonate. (This we found preferable to milk, which is commonly used for standardising pancreatin.) 2 Cc. of an active Pancreatin Solution were then added. We had, therefore, the equivalent of an average dose of the "drug" in 570 Cc. (1 pint) of liquid, this bearing some relation to the conditions *in vivo*.

Conclusions.—The table of results showing compatibility, or the reverse, after 1 hour at 40°C ., on examination with Nitric Acid for Albumin in the usual manner, is given in the Edn. XVII., p. 126. We repeat our general conclusions:—

Notable *incompatibles* were *Acids*, in general, *Alcohol*, *Calcium Chloride*, *Ferric Chloride*, *Manganese Sulphate*, *Manganese Hypophosphite*, *Quinine Hydrochloride* and *Bi-hydrochloride*, and *Syrup of Ferrous Iodide*.

The information is important in regard to the prescribing of Pancreatic Extracts with other preparations and with regard to effects *in vivo* when the above medicines are given.

Cf. also Pepsin Results, *postea*, and 'Enzyme Action,' Vol. I., p. 662.

EXPERIMENTS TO DETERMINE EFFECT OF CHEMICALS ON THE AMYLOLYTIC ACTION OF PANCREATIN.

It seemed of interest to determine the amylolytic activity of a *Pancreatin* which had been found to be weak in proteolytic power and then subsequently to determine the inhibitory effect of drugs on the amyolysis.

With regard to the first point it was found that the sample of Pancreatin in question was well up to standard when tested for amylolytic power; and a liquid preparation of commerce, which had strong proteolytic power, was found to be practically useless for amyolysis. *Cf.* Malt Diastase results.

As to the second point, 0.4 Gm. of the Pancreatin, weak in proteolytic power, was mixed with 10 Cc. of Water, and added to Starch 7.5 Gm. gelatinised in water 150 Cc. (made almost transparent by boiling and cooling)—the amount of medicament having been previously added to this Starch mixture.

After 5, 15 and 30 minutes the liquors were tested with dilute Iodine Solution on the lines of the U.S. Assay Process. Results were as follows (—meant inhibition of activity, + compatibility):—

			5 minutes.	15 minutes.	30 minutes.
Acid	Aceto-Salicylicum	0.16 Gm.	—	—	—
„	Hydriodicum Dil.	0.15 Cc.	—	partial.	partial.
„	Hydrobromicum	0.5 Cc.	—	—	—
„	Hydrochlor. Dil.	0.15 Cc.	—	—	—
„	Salicylicum	0.16 Gm.	+	—	—
„	Tannicum	0.16 Gm.	—	—	—
Alum (Potash)		0.16 Gm.	partial.	partial.	+
Caffeinæ Citras		0.08 Gm.	partial.	partial.	+
Ferri Perchloridum		0.1 Gm.	—	—	—
Piperazine		0.16 Gm.	—	partial.	partial.
Potassii Bicarbonas		1.3 Gm.	+	—	—
Syr. Ferri Iodidi		0.6 Cc.	+	—	—

Some commercial varieties of Pancreatin yield to peptonised milk an objectionable odour.—T. E. Tawell points out that this is due to the fact that the cheap forms of Petroleum are used in extracting fat from Pancreatin.—P.J. ii./13,570.

Muller's Trypsin Test.

A method of testing the activity of Trypsin preparations consists in placing small quantities of the Trypsin preparations to be tested from a Platinum loop, upon a Löffler Blood Serum plate and incubating 12 hours at 55 to 60° C. In good products a depression should be made on the Serum with a dilution 1:1000.—Pr., Jan., 1913. See also Sorensen's Test, P.J. ii./12,137 and B.M.J. i./12,584.

PARAFFINUM LIQUIDUM (B.P. '14).

(See also Vol. I., p. 655.)

Viscosity of Liquid Paraffin.

The introduction of a wider range in Sp. Gr. in B.P. '14 led to the wrong type of 'Oil' being employed as an intestinal lubricant. An 'Oil' with a Sp. Gr. of 0.860 is more of the nature of Petrol than Liquid Paraffin. It passes too rapidly through the system. A light spirit could be positively injurious by reason of its caustic solvent nature.

The determination of its *viscosity* by the **Redwood Standard Viscometer**—an apparatus devised by the late Sir Boverton Redwood, for the proof of suitability of oils for lubricating various types of machinery—is therefore of importance. Viscosity is as important as Sp. Gr., because viscosities may vary when Sp. Grs. are the same. In a series of Liquid Paraffins examined by the *Lancet*, viscosities at 100° F. varied from 440 to 67 seconds.

The **gravity should be as high as possible, at least 0.880, and the viscosity at least 180.** The meaning of this is that in the viscometer 50 Cc. of Oil **takes at least 180 seconds to flow out.**

H. B. Russell and P. C. Brett have recommended a viscosity of at least 180.—v. Vol. I., p. 655. A sample of a *good* Liquid Paraffin examined by the author had Sp. Gr. 0.884 and viscosity 250, while a relatively inferior one had Sp. Gr. 0.876 and viscosity 118.

Both were free from **Sulphur Compounds** and fluorescence, which are also important factors.

The B.P. **Sulphuric Acid** test should also be watched—some of the poor quality oils give a *black* colour with it.

It may also be mentioned that **chemically, Russian and American Oils differ**—the former being in general genuine Paraffins—saturated hydrocarbons as distinct from unsaturated olefines (cf. Vol. I., pp. 53, 655), but for internal use it is doubtful whether there is any difference on this score.

Wij's Solution employed with a Liquid Paraffin (variety not stated), showed I.V. *nil*—no iodine absorbed. *Soft* Paraffins on the other hand gave I.V.'s ranging from 2.8 to 12.4.—W. R. Pratt & H. L. Smith, P.J. ii./15,544.

DESCRIPTION OF VISCOMETERS.—C. W. Gosling, P.J. ii./22,87.

Liquid Paraffin may be used for **lens immersion**.—Rowntree.

A good mounting medium for Bacteria. The refractive index of bacteria is said to be 1.55, Canada Balsam 1.538, Balsam in Xylol a little lower, say, 1.53, Distilled Water 1.336, Liquid Paraffin 1.471. In a medium exactly that of the bacteria, *e.g.*, Oil of Aniseed 1.55, the bacteria, dried, but unstained, would be invisible, in Canada Balsam they would be seen, in Paraffin better and in Water best. Of all practical media Parolein was found to be best for organisms with flagella. Liquid Paraffin is, however, not so good as Cedar Wood Oil for lens immersions.—A. C. Coles, L. i./11,877.

'Petrol' and Petrol Tests.

Petroleum or Motor Spirit (Gasoline in U.S.A.)

This is the lowest boiling commercial fraction of crude petroleum and has, in the U.K., a Sp. Gr. of about 0.72 to 0.75. The boiling range is from about 35° C. to about 195° C., with approximately 40% distilling at 100° C. In the U.S.A. the boiling range is somewhat longer.

Aviation Spirit—A definitely lighter gravity is used with an end point of about 150° C. to 160° C., and is admixed frequently with twenty or more per cent. of Benzol.

Petrol is a complex mixture of various hydrocarbons mainly saturated and of the paraffin, aromatic and naphthenic types, but at the present time more and more is being obtained by the cracking of the heavier hydrocarbons in petroleum resulting in the formation of cracked gasoline that contains very considerable amounts of the olefine series.

To cope with modern high compression engines, Benzol is frequently added to Petrol and may be estimated, by the increment of specific gravity it causes and by its effect on the critical solution temperature in aniline.

Coal, and other solid fuels, are converted into liquid fuels (Petrol, Diesel oil, and heavy fuel oil) by "**Berginisation**," a process of hydrogenation under pressure (over 100 atmospheres) at high temperatures (400–500° C.).

Exhaust gas in car, poisonings by, L. i./20,1334.

Although **Gasoline** (virtually Petrol) **Vapor** has an intoxicating effect the toxicity of a given amount is much less than that of Carbon Monoxide produced by its incomplete combustion in an engine. Experiments on dogs. The anæsthetic action of Gasoline Vapor is somewhat like that of Ether, but with marked convulsant effects, due doubtless to irritation of the cerebral cortex.—H. W. Haggard, Jl. Pharm. & Exp. Therap., Dec., 1920.

EXHAUST GAS from petrol engines for destroying rats has advantages.—D. B. Blacklock, L. ii./24,568.

National Benzol Mixture consists of Empire-produced Petrol mixed with a variable quantity of Coal Tar Benzol, dependent on the amount of aromatic bodies already present in the Petrol, to produce a Petrol possessing a high useful compression ratio (h.u.c.r.). The mixture usually contains at least a third of its volume of Benzol. Stated to be economical. It produces power, speed and smooth running; it forms little carbon; it is anti-pinking, unrivalled for hill-climbing, volatile, clean, and gum-free.

Benzol, detection of, in light Petroleum. A reagent is made by mixing equal volumes of Alcohol 95% and aniline. On adding 2 Cc. of this to 5 Cc. of light Petroleum, the aniline separates and forms a distinctive layer. If it contains 5% C_6H_6 , a perfectly clear solution results. If less than 5% is suspected the Petroleum should be fractionated and the test used on the 80–110° C. fraction.—Y.B.P. '23,184.

White Soft Paraffin. The Iodine value varies between 10 and 40, whereas for the yellow it is about 40.—E. G. Bryant, B.P.Conf., 1926, P.J. ii./26,196; C.D. ii./26,257.

Hard Paraffin can be determined in oil and wax mixtures by its *insolubility* in Acetone.—Analyst, '26,105.

PEPSINUM.

B.P. '14.—Pepsin standard requires that one part digests 2,500 of hard boiled egg albumen, with certain conditions.

Further Assay Methods :—

FR. CX. requires that the Pepsin shall convert 25 times its weight of dried fibrin. Pepsin 0.1, Dilute Hydrochloric Acid 1.5, Water 58.5, Fibrin 2.5 for

9 hours at 50°. Test filtrate with Nitric Acid. Pepsin Amylacée and Pepsin Lacrosée in dose 0.25 Gm. are to contain sufficient Pepsin to carry out the above test.

Hercood and Maben, comparing the official methods in various countries, suggested an International Standard 1 to 2,000 and *Assay Method* as follows :

Coagulate white of egg (obtained by boiling fresh eggs for ten minutes), pass through a No. 40 sieve, and press between two sheets of filter-paper to remove surplus moisture ; place 10 Gm. in a 200 Cc. flask containing 100 Cc. of distilled water previously heated to 52° C., 0.25 per cent. absolute HCl, and 5 Cc. of a 0.1 per cent. solution of pepsin. Place the flask in a water-bath at 52° C., and digest at that temperature for two hours, stirring gently every fifteen minutes with a rotatory movement by means of a glass rod. At the expiration of two hours the albumin should be dissolved, the solution having an opalescent appearance.—P.J. ii./10,368 ; C.D. ii./10,371.

Carmino-fibrin, prepared by washing blood fibrin with ammoniacal solution of carmine, is a dark coloured mass, easily crumbled, which yields no colour to water or 0.1% Hydrochloric Acid until the fibrin contained in it has been dissolved by a ferment ; hence its use as a simple quantitative test for pepsin by noting the time required to give a pink colour equal to that of a standard or control.

THE EFFECT OF CERTAIN CHEMICALS AND DRUGS ON THE ACTION OF PEPSIN.

The following experiments which we conducted show approximately the relative inhibitory action *in vitro* which certain chemicals and drugs have on the digestive power of Pepsin. The conditions under which the experiments were conducted were :

Three Gm. of Egg Albumen, prepared as for testing Pepsin (*Off.*), were placed in 30 Cc. of Hydrochloric Acid 0.2%. An average dose (in most cases) of the drug was added, followed by 1 Cc. of freshly prepared Pepsin Solution containing 0.2% of Pepsin (*Off.*). These mixtures were then incubated at 38° C. for fifteen hours, this length of time being allowed to permit of the Pepsin utilising its power to the utmost. It is to be noted that 30 Cc. of fluid is a small amount in comparison with the capacity of the human stomach, but the results are comparable, and it is evident that if the drugs in question do not interfere with peptic activity in this strong concentration, they are certainly not likely to do so when more diluted. On the other hand, if peptic activity is interfered with, there is evidence of physiological incompatibility.

The following apparently **do not interfere** with peptic activity to any extent :—

LIST A.

Acidum Benzoicum.	Elixir Papain.	Magnesii Sulphas.
„ Boricum.	Ext. Cascaræ Liq.	(small dose)
„ Cacodylicum.	„ Cinchonæ Liq.	Migralgin.
„ Carbolicum.	„ Cocæ Liq.	Naphthalini HCl.
„ Hydrochloricum.	„ Ergotæ Liq.	Pancreatinum.
„ Hypoph. Dil.	„ Hydrast. Liq.	Phenactinum.
„ Phosphoricum.	„ Ipecac. Liq.	Phosphorus.
„ Salicylicum.	„ Nucis Vom. Liq.	Physostigmin. Sulph.
Æther.	Guaiacol Camph.	Picrotoxinum.
Alcohol, small amount.	„ Carbonas.	Pilocarpinæ Nitras.
Aspirin.	Heroin Hydrochlor.	Podophyllin.
Caffeinæ Citras.	Hydrarg. Perchlor.	Pyramidon.
Calci Glycerophosph.	„ et Pot. Iod.	Sodii Arsanilas.
Chloromorphiæ Liqueur.	Hydrogen. Peroxid.	„ Cacodylas.
Chloroformum.	Hyoscine HBr.	Syrupus Ferri Iodid.
Cocainæ Hydrochlor.	Liq. Arsen. Hydrochl.	Theobromina.
Codeinæ Hydrochlor.	„ Hamamelidis.	Thiosinamin.
Elizir Aromaticum.	„ Morphinæ Hydrochl.	

In arriving at the above conclusion we took, in most cases, 6.6%, or less of Albumen, *undissolved*, to indicate in the conditions of the test **physiological compatibility**. The gradation of figures in respect of different amounts of Alcohol (using 0.6 Cc. of 90% Alcohol 8% of the Albumen ; with 4 Cc. 13%, with 8 Cc. 33%, with 15 Cc. 88%) was particularly interesting and instructive. The fact that **Acids** in general other than Hydrochloric

are compatible is of interest. The compatibility of **Chloroform** is well known. Other interesting and perhaps unexpected *compatibles* are **Creosote**, **Ether**, **Guaiacol preparations**, **Mercuric Chloride** (in a therapeutic dose), **Hydrogen Peroxide** and **Sodium Arsanilate**.

The following chemicals are only compatible when present in a dilute form, that is in a volume of Liquid bearing more resemblance with that encountered in the human digestive tract.

For this purpose the drugs (see 17th Edn.) were treated as follows :—

14.2 Gm. Egg Albumen prepared as before were placed in 150 Cc. of Hydrochloric Acid 0.2% containing 10 mgr. of Pepsin and $\frac{1}{4}$ of an average dose (in most cases) of the drug was added.

The results were as follows :—

LIST B.

Chemical or Drug.	Undis- solved Albumen after 15 hours.	Chemical or Drug.	Undis- solved Albumen after 15 hours.
Alum 0.15 Gm. . . .	Nil.	Mag. Sulph. 1 Gm. . .	5 Gm.
Cupri Sulphas 0.1 Gm. . .	Nil.	Paraldehyd. 0.5 Cc. . .	Nil.
Ext. Malti Liq. 2 Cc. . .	Nil.	Phenazone 0.15 Gm. . .	Nil.
Fel Bovinum 0.15 Gm. . .	0.4 Gm.	Piperazina 0.15 Gm. . .	Nil.
Ferri et Amm.Cit. 0.13 Gm.	Nil.	Potassa Sulph. 0.1 Gm.	0.5 Gm.
„ et Quin. Cit. 0.13 Gm.	Nil.	Sodii Nitris 0.02 Gm. . .	Trace
„ Perchlor. 0.1 Gm. . .	Nil.	„ Sulphis 0.15 Gm. . .	Nil
„ Sulphas. 0.05 Gm. . .	Nil	Thiocol 0.15 Gm. . . .	Nil.
Helmitol 0.15 Gm. . . .	Nil.	Zinci Brom. 0.05 Gm. . .	Nil.
Hexamine 0.15 Gm. . . .	1.7 Gm.	„ Sulphas 0.02 Gm. . .	Nil.
Liq. Amm. Citrat. Fort. 1 Cc.	11.5 Gm.	Control	Nil.

Conclusions.

Dilution of the chemical or drug plays an important part.

'List B' shows that in a large volume of fluid the substances incompatible with Pepsin are relatively few, but the result with **Magnesium Sulphate** is of interest.

Nature might compensate effects produced by chemicals in a manner which it is impossible to imitate in such experiments.

At the same time one cannot overlook that under certain conditions, *e.g.*, ill health, or an empty stomach, the volume of diluent fluid might be greatly reduced. These results may be compared with the Pancreatin and Malt Expts.

See also 'Enzyme Action,' Vol. I., p. 662.

PHENOLPHTHALEIN and FLUORESCEIN COMPOUNDS.

(See also Vol. I., p. 677.)

New Iodo derivatives of phthaleins. Octoiodophenolphthalein described.—Am.Jl.Pharm., June, '28, 374.

Tetra-iodo-phenolphthalein is described Vol. I. A death followed oral use but in reality it was a case of rupture of the liver capsule from pressure.—G. E. Dyas, B.J.R., Mar., '28, 97. Sir W. H. Willcox, *ibid.* June '28, 219.

Phenoltetrachlorphthalein. $\text{C}_6\text{Cl}_4 \begin{array}{l} \swarrow \text{C}(\text{C}_6\text{H}_4.\text{OH})_2 \\ \searrow \text{CO} \end{array} \text{O} = 455.908.$

Dose.—8 Cc. of a 5% solution, *i.e.* 0.4 Gm., in the form of the Di-Sodium Compound, intravenously. (N.N.R. per Y.B.P. '23, 429, states from 0.05 to 0.4 Gm.)

It cannot be given subcutaneously or intramuscularly.

This compound has been employed as a test for *liver function*. When given subcutaneously (in animals) it escapes exclusively *via* the biliary passages. Resorption from the large gut occurs to a slight extent, but since the action

of the substance itself is purgative, very little absorption takes place. The excretion of the chemical diminishes in proportion to the amount of liver tissue damage.

Technique.—A 5% solution is made by boiling 2.5 Gm. with 5 Cc. of 2 N Sodium Hydrate and water sufficient quantity to 50 Cc. The night prior to the test a purgative is given, and on the morning following 8 Cc. of the solution is given intravenously.

The stools are collected for 48 hours after. The patient must be purged throughout the test. The faeces are shaken 20 minutes with 1 to 1½ litres of water, and one-tenth of the volume is decanted. 5 Cc. of 40% Sodium Hydrate are added. The mixture turns red. After thorough shaking, 100 Cc. are decanted into a 200 Cc. flask containing 5 Cc. of Saturated Basic Lead Acetate Solution, 5 Cc. of 40% Sodium Hydrate are added and the volume made up to 200 Cc. The colour should not be deepened by more Soda. The solution is now allowed to stand a short time, for the supernatant fluid to clear. In the meantime, a standard solution of the dye is made by taking 0.4 Cc. of the original 5% solution, adding sufficient Sodium Hydrate to make a permanent colour and water to 1000 Cc. Small portions of the two liquids are now compared. The percentage recovery of the dye can thus be found. Any recovery below 30% is regarded as pathological.

The test is said to give satisfactory information in advanced cirrhosis, cancer, and syphilis affecting the liver.—Beaumont & Dodds; Rowntree and Co-workers.

Chemical Notes.—Phenoltetrachlorophthalein is a stable body. It occurs as a white powder, insoluble in water but dissolving to a deep red solution with caustic alkalis. (It has been suggested to replace Phenolphthalein as indicator for alcoholic solutions.) The alkaline solution is liable to take up CO₂, diminishing the strength slightly.

Content of Tetrachlorfluorane should not exceed 0.2% and Ash 0.15%.—Jl.A.M.A., '23,80,1218, Y.B.P., '23,429.

Normally it is removed rapidly by the liver from the blood. A damaged liver takes up the dye more slowly. 5 mgr. per kilo intravenously is employed. Normally, 2 to 6% is present in the plasma 15 minutes after, and disappears entirely in 40 to 60 minutes. Comparison of blood samples is made with a solution of 10 mgr. of the dye in 100 Cc. of water. Results express how much of the total amount of dye is present in the blood stream.—S. M. Rosenthal, Jl.A.M.A., 1922,79,2151, Y.B.P., '23,59. See also Pres., Feb., '23,76.

The test is more delicate than the urobilinuria method and more reliable than the hemoclastic crisis test, or the Levulose tolerance test, which latter was of little practical value. Thrombosis might be obviated by smaller injection than that recommended (5 mgr. per kilo). **Bromsulphalein** similarly employed gives more sharply cut results.—B.M.J. i./25,272.

Clinical tests for hepatic function.—C. H. Greene, Jl.A.M.A. ii./25,1476.

Estimation of the Phenoltetrachlorophthalein left in the blood after an interval shows that function of the dye is less pronounced with cancer than with cirrhosis. In cases with enlarged liver, retention of dye suggests cancer rather than hepatitis or cirrhosis.—Per Jl.A.M.A. ii./25,1008.

Phenoltetrabromphthalein Sodium Sulphonate. *Syn. Bromsulphalein.* 5 mgr. per kilo injected intravenously, is also most suitable.—S. M. Rosenthal and E. C. White, Jl. Pharm. Exp. Therap., '24,287; Pres., June '25.

It is almost entirely eliminated by the liver, but in cases of retention in the blood stream the dye may be eliminated in the urine from traces up to 20% of the amount injected.—W. J. Kerr and Co-workers, Jl.A.M.A. ii./25,942.

Cases of liver disease show retention of dye representing fairly accurately the degree of liver damage or functional impairment—100% retention means that no dye is removed from the blood, and 50% would mean that the liver was 50% incompetent, and so on. The test is one of liver function and not biliary permeability. It is safe, simple, and appears to be the best we have.—E. Bulmer, L. ii./28,326.

Of 20 cases with early liver disease the Lævulose tolerance test was positive in 16 while the Bromsulphalein content of the blood serum 5 and 30 minutes after injection showed normal. The five minutes' interval retention of the dye does not afford much information in early liver disease, nor does the retention of the dye run parallel with the Bilirubin retention.—A. D. Fraser, L. ii./28,654.

Rose Bengal Liver Function Test.

Rose Bengal can be either the Potassium salt of Tetraiodo-di (or tetra-) chlorofluorescein, or of hydroxy-tetraiodo-di (or tetra-)ortho-carboxy-phenylfluorone, or the Sodium salt of the two dichloro compounds.

It can be obtained by the action of Iodine on Dichlorofluorescein in the presence of Potassium Chlorate and Cupric Chloride (dichloro compound), or by acting on tetrachlorofluorescein with Iodine to produce the tetrachloro body.

It is a dark or brownish red powder soluble in water without fluorescence.—Colour Index, 1924.

Technique.—Withdraw sample of blood from vein in the cubital fossa and discharge into graduated centrifuge tube containing 2 Cc. 2% Potassium Oxalate solution. Without removing needle from vein inject 100 mgr. of dye (150 mgr. in large persons) in sterile 1% Salt solution. Leave needle in vein and 2 minutes after injection withdraw 10 Cc. blood from needle (still *in situ*) into a fresh syringe and discharge into another centrifuge tube containing 2 Cc. Oxalate solution: repeat this at 4 and 8 minutes after dye injection. Withdraw needle and leave patient in darkened room for an hour. Centrifugalise blood samples at 2,000 revs. for $\frac{1}{2}$ hour, and note percentage of cells and plasma in each tube. From the last three samples dilute 3 Cc. plasma in separate tubes with equal volume Salt solution and compare colour in a Hellige colorimeter with standard solution containing 5 Cc. plasma from first tube and 5 Cc. of a 0.0075% solution Rose Bengal. The colorimeter reading is corrected to allow for the 2 Cc. Oxalate solution. Having obtained the concentration of the dye in the 2-minute sample, and knowing the total amount of dye injected, calculate the blood volume of the person. For the purposes of comparison, a standard blood volume of 7,000 Cc. is taken, and the final concentration is obtained by multiplying the corrected reading by the blood volume and dividing by 7,000.

The dye is eliminated almost entirely from the blood stream through the liver. It remains in the circulation for a sufficient length of time for determination of the dye in the plasma to be made. Patients with definite cirrhosis or other extensive liver disease show marked retention of the dyes in the blood. The test may be of great value when jaundice and ascites are presenting symptoms. Technique described.—W. J. Kerr and Co-workers, J.I.A.M.A. ii./25,946. See also J.I.A.M.A. i./27,1620.

Sodium Salicylate as Liver Test. Normally, the liver transforms $2\frac{1}{2}$ grains, so that none is found in the urine by Ferric Chloride during 5 hours following the dose. A violet ring at zone of contact indicates inefficient function. Give the dose 1 hour after breakfast.—Y.B.P., '23,63.

Van den Bergh Reaction, see p. 611.

PINUS.**Oleum Terebinthinæ.**

(See also Vol. I., p. 699.)

Lævo-Pinene or **Terebentene** of Berthelot is obtained by fractionation of French Oil of Turpentine as a colourless mobile liquid of characteristic odor. Sp. Gr. 0.8767 at 0° C. and 0.8619 at 17.9° C.

Dextro-Pinene or **Australene**, the principal constituent of American Turpentine has the same Sp. Gr. and boiling point, etc., as the French. O.R. is stated to be + 2.15°.

Russian Turpentine Oil.—Authentic samples contain 40 to 70%, distilling between 155° and 160° C. and consisting chiefly of Pinene. The oils arriving in the London markets have these 'middle runnings' removed.

For MAKING DISINFECTANTS it may not be of importance to have a large amount of hydrocarbon of relatively low boiling point. Useful details tabulated.—E. J. Parry, C.D. ii./12,340,655; Y.B.P., 1913, 93.

Indian Turpentine from *P. Longifolia*, Constituents of.—J. L. Simonsen, J. C. S. May, '20, 570.

Oregon and Colorado Douglas Fir Oils from trees grown in Britain. Geraniol the chief odorous constituent of the first. The odour of the other appears due to the large % of pinene and bornyl acetate.—C. T. Bennett, P.R. 1920, 218.

Abietic Acid derivatives and decomposition products.—J.C.S.A. i./20,232.

PIX LIQUIDA (B.P. '14).

(See also Vol. I., p. 703.)

Stockholm Tar is a peasant-made article; this tar can be separated by fractional distillation into three principal fractions: (1) A watery portion containing pyroligneous acid, methyl alcohol or wood naphtha, and acetone; (2) **light oil of tar** which contains some of these substances Toluol, Xylol, and other hydrocarbons of that series; and (3) **heavy oil of tar** which contains phenols, creosol and guaiacol. The redistillation residue is ordinary block pitch. It has been arranged to define wood tar made by burning the roots of the Swedish pine tree (*P. Sylvestris*) in the peasant way—so-called '**Dalbrand Tar**' as 'genuine Swedish peasant-made Tar' and that 'Factory Tar' of Swedish origin shall in future be called '*Swedish Kiln Tar*.'—C.D. ii./13,331. See also D. McEwan, C.D. i./11,264.

Rectified Oil of Tar.—One gallon of Stockholm Tar yielded only a few ounces of oil with Sp. Gr. 0.921, but American Wood Tar Oil yielded nearly 40% of a brown oil with characteristic tar odour having Sp. Gr. 0.920. This redistilled with soda gave a colourless oil with faint Terebene odour and Sp. Gr. 0.881 and flash point 124° F. Commercially it is made from imported tar oil from Russia, Sweden and America by distilling and refining here. E. J. Millard, P.J. i./18,28.

Oleum Cadinum.

The following **Characters and Tests** have been suggested:—

A vegetable tar obtained by dry distillation of *J. Oxycedrus*, of brownish red colour, transparent, clear and homogeneous aspect, has a wood-smoke-like odour, with a density lower than water. It is almost *insoluble* in Water, but gives it an acid reaction, partly soluble in cold Alcohol, completely soluble in hot Alcohol (90%), in Ether, Chloroform and Carbon Bisulphide. The acidity expressed as Acetic Acid must not exceed 1.5 per 100 Cc. It must be free of other Tars and particularly not give the **Copper Acetate Test for foreign Wood Tars and Resins.**—Shake out with Petroleum Ether, filter and shake filtrate with equal volume of 1% solution of Copper Acetate. the Petroleum layer is coloured green if wood tar be present. A test on these lines is adopted, B.P. '14, to ensure absence of *Pine Tar*.

We found on testing an assumed genuine sample, which gave no indication by itself, that *at least* 20% of Wood Tar (Stockholm) had to be added to give a definite green color to the dark supernatant liquor. There was no appreciable difference between the sample and the same adulterated with 10% of Stockholm Tar. Oleum Betulæ Pyroligneum gave a deep olive green color. Creosote, Phenol and Oleum Picis Rectificatum were tested and found to give no colour at all.

PLUMBUM.**Lead Poisoning.**

Lead Paint Regulations 1927 (S.R. & O. 1927, No. 847), under **Lead Paint (Protection against Poisoning) Act 1926** (16 & 17 Geo. 5, c.37).

Lead paint for buildings must be in **paste form** or **paint ready for use** (but red lead may be had raw or dry for stopping or filling). Must not be used in form of spray in interiors. Surfaces other than iron or steel must not be rubbed down or scraped by dry process, except if the surface contains no lead.

Lead poisoning amongst yarn workers.—B.M.J. i./o6,310.

Lead poisoning and the race.—Amongst a host of facts and fancies put forward, the following appears. Where (in Hungary) death from convulsions in early infancy rarely occurs, epilepsy is found later on to be more frequent in the children of potters than in those of non-potters.—B.M.J. i./11,1096.

Lead poisoning in all forms well treated by Calcium Permanganate in doses of $\frac{1}{4}$ grain.—B.M.J., May 14/10,1166.

English Potteries, Lead Poisoning in, Home Office Report on.—B.M.J. ii./11,44.

In industries using lead where much dust occurs lead poisoning is frequent, —the main avenue of entrance of the poison being the lungs.—T. M. Legge and Sir K. W. Goadby.—B.M.J. ii./12,1712; L. i./13,183.

Determination of Lead in Lead Salts—Lead Acetate and Liquor Plumbi Subacet. Fort.—R. L. Morris, C.D. '19,242.

Soluble lead in Casseroles.—H. Masters, L. i./20,1394.

BRONCHIAL ASTHMA possibly attributable to use of hairwash containing Lead, also to persons exposed to White Lead dust and Lead workers abroad. Saturnine asthma in this country is practically unknown among Lead workers.—Sir Thos. Oliver, L. ii./22,907.

FACE ENAMEL caused poisoning.—M.P.C., Nov. 29/22,451.

BEER.—Cases at Isleworth due to lead glaze enamel on iron tanks; 93 persons affected.—M.P.C., Oct. 4/22,295.

Lead poisoning included in France, in October, 1919, among the liabilities of employer's and workmen's compensation insurance agencies. As a result of the examination of 179 workers—apparently healthy—exposed to lead poisoning, the lead line was found in 65%. The LEAD LINE is not a uniform or reliable sign of lead poisoning. Early and accurate information can only be obtained by demonstration of lead in the urine and basophil granules in the red corpuscles.—A. Feil and R. Heim de Balsac, per L. i./23,1325.

Lead Oxide poisoning as an ABORTIFACIENT. Doses of 1 to 2 teaspoonfuls, used in Copenhagen, have caused prolonged ill-health.—B.M.J.E. i./24,57.

A Test for Lead Absorption.

In normal persons the number of basophilic cells per Cc. of blood as a rule is less than 1,000 and never exceeds 5,000. Lead poisoning produces counts over 7,000 and up to 100,000, but symptoms may not occur even when the count is as high as 60,000 to 80,000. When a worker who is exposed to Lead develops a basophilic red cell count over 6,000 or 7,000, and when other conditions which might produce such a count are absent (certain physiologic states—Benzene poisoning, Arsenic poisoning, all types of anæmia in which there is regeneration, hæmolytic icterus, the condition following hæmorrhage, leukæmias, acute infections, neoplasms involving bone marrow and polycythemia—increase the proportion of basophilic cells up to 20,000) the worker should be considered a Lead poisoning prospect.—Jl.A.M.A. ii./28,251.

DISTRIBUTION AND STORAGE OF LEAD IN THE ORGANISM.—It has been shown that lead is retained indefinitely in the solid portion of the bones. Such lead is harmless, but is held at a point where its liberation would flood the organism with toxic soluble lead. A depleted alkali reserve tends to mobilise the stored lead.—A. S. Minot and J. C. Aub., Jl. Ph. Exp. Ther., Mar., '24/159.

Determination of small amounts of Lead in animal tissues.—Analyst, 25,46.

No diagnostic value in qualitative Lead determinations in urine or fæces as most persons have absorbed appreciable quantities. There is no quantitative expression of Lead secretion in man significant of impending or present Lead poisoning.—R. A. Kehoe and Co-workers, Jl.A.M.A. ii./26,2084.

RED PEPPER containing 20.5% Red Lead and 4.1% Sand caused 314 cases of Lead poisoning, with three deaths, in Bulgaria.—L. ii./26,507.

SNUFF wrapped in tinfoil caused three cases of chronic poisoning.—J. Uttal, Jl.A.M.A. i./28,290.

Plumbism and its avoidance. Lead painting more likely to harm women than men. Consideration of the Lead Paint (Protection against Poisoning) Bill.—L. ii./26,1119,1132,1144.

Spraying Paint or Lacquer.—The practice of spraying paints or lacquer containing over 1% of Lead should be discontinued, or carried out only where adequate air movement is provided. Similarly, the amount of Benzol used in lacquers should be limited to 0.5%. Definite *silicosis* hazard from spraying of vitreous enamels.—L. ii./28,177. See Lead Paint Regns. at commencement of Chapter.

Lead is absorbed most easily through the respiratory tract, and as little as 1 to 2 mg. daily is likely to produce chronic poisoning. It may be stored in the skeleton or eliminated by excretion and may be carried in the blood stream as Colloidal Lead Phosphate and deposited as tertiary Lead Phosphate. When

Lead is generally distributed throughout the organism it is desirable to facilitate storage with an ample Calcium intake. After acute toxic symptoms have passed elimination is helped by low Calcium intake. A danger exists in the use of containers glazed or soldered with Lead compounds.—Jl.A.M.A. ii./25,2034.

'Ethyl Gas.' *Further data, Vol. I., p. 659.*

A type of gasoline containing Lead Tetraethyl, $Pb(C_2H_5)_4$, also known as "Ethyl Fluid," an "antiknock" dope or compound supplied to the motoring public in some States of the U.S.A., which when mixed with low-grade gasoline gives a motor petrol free from the disability of "knocking" or "pinking." Lead Tetraethyl is a poison of terrible potency, 500 times as convulsant as Strychnine, the fumes of the pure product being comparable in deadliness with undiluted Hydrocyanic Acid. Even the gasoline dilution (about 1 in 1000) is not free from danger. Carbon Tetrachloride is used with the Lead Tetraethyl to prevent the deposit of lead on the sparking plug during combustion. Carbon Monoxide has led to fatalities in garages—What will be the effect of unburnt Ethyl Gas, or, if burnt, of Lead fumes? A very risky experiment.—C.D., Feb. 2/24,162.

Chemical Characters.

Lead Tetraethyl is a liquid boiling at $150^\circ C.$ with decomposition. It is manufactured by treating Lead Tetrachloride with Methyl Magnesium Iodide. The products of combustion are: (1) with excess air—chiefly Carbon Dioxide and Lead Oxide, (2) with deficiency of air (*e.g.*, in engine cylinder)—chiefly Carbon Monoxide and Lead. It is not very volatile at ordinary temperatures.—P.J. i./28,268.

Lead-poisoning due to the manufacture, etc., of Tetraethyl Lead. The condition bears little resemblance to clinical types of lead-poisoning. It is not immediately corrosive, but causes necrosis after lengthy exposure. If allowed to remain on the skin for half an hour no sensation is produced but desquamation occurs after a day or two. Poisoning results from a combination of skin absorption and inhalation of vapour. The inhalation of dust has also caused illness.—R. A. Kehoc, Jl.A.M.A. ii./25,108.

Post-mortem findings in 4 cases of poisoning. A volatile lead compound was proved in the brain tissue. All the organs, including the blood, contained lead.—C. Norris and A. O. Gettler, Jl.A.M.A. ii./25,820.

Determination in motor fuels of Lead Tetraethyl.—Analyst, '26,104.

Ethyl Petrol coming into this country from the U.S.A. contains 6 Cc. Ethyl Fluid per gallon. The Ethyl Fluid consists of Lead Tetraethyl 54.5%, Ethylene Dibromide 36.5%, Monochloronaphthalene 9%, with a trace of Sudan IV.—Nature, Mar. 17/28,424, per P.J. i./28,321.

Interim Report of Departmental Committee of Min. Health (Report issued July 27, 1928). There is no evidence that the use of Ethyl Petrol involves more danger to health than the ordinary, but the precautions suggested by the U.S. Committee should be carried out, *e.g.*, labelling of cans and pumps, leaflets, and dyeing of the substance red. Warning against use for purposes other than as motor fuel, *e.g.*, cooking and cleaning. In no case does the amount of Lead Tetraethyl in commercial spirit exceed 1 in 1,300 by volume or 1 in 650 by weight. The deaths in the U.S.A. not attributed to the diluted mixture (Ethyl Petrol). Drivers and garage employees in U.S.A. gave no definite signs of poisoning after exposure for 2 years.—B.M.J. ii./28,219.

In view of the difficulty of recognising poisoning by Lead Ethyl, we should protest against the use of Ethyl Petrol. Are we to put a higher value on a slightly increased efficiency of engines than on a certain, even if slight, impairment of the health, efficiency and longevity of our exquisite bodily machinery?—F. C. Eve, B.M.J. ii./28,222.

PODOPHYLLI INDICI RHIZOMA.

See also Vol. I. p. 707. (Podophyllum Emodi.)

Physiologically *P. Emodi* is quite as active as the American *P. peltatum*. Picropodophyllin to the extent of 5.43% was obtained from Indian root collected after flowering, corresponding to an equal weight of Podophyllotoxin (with which it is isomeric). The resin yield was 10.79%—indicating a proportion of 50.3% of Picropodophyllin, whilst that in *P. peltatum* averages

only about 20—25%. *Picropodophyllin* is not an actual constituent of the drug, but is formed by decomposition of *Podophyllotoxin*, which, together with *Podophyllo-resin*, an indefinite amorphous substance, represents the activity of the drug. 'Fall-dug' *P. peltatum* is preferred in America.—Umney, P.J. ii./11,156; C.D. ii./09,335.

T. A. Henry found that the action of both is due to *Podophyllotoxin* (purgative) and *Podophyllo-resin* (purgative and cholagogue). The Indian is richer in the former. Estimation process for *Podophyllotoxin*.

P. Emodi roots from the N.W. province of India gave 11.07 and 11.17% total resin. The proportion of *Podophyllotoxin* was in the first case 4.7%; in the other 3.1%.—P.J. ii./12,579.

PODOPHYLLI RESINA.

Reaction of *Podophyllum peltatum* and *P. Emodi* *Podophyllins* towards Ammonia is of interest. If 0.5 Gm. of Resin be well stirred with 5 Cc. of Dilute Ammonia and 5 Cc. of water, and after 20 minutes the solution be filtered the residue washed and dried near 100° C., should not weigh more than 0.13 Gm., i.e. 26%, if the resin has been made from *P. peltatum*.—D. B. Dott, P.J. ii./18,318 (per Y.B.P. 1919,99).—cf. B.P. '14 Test.

The Resin from *P. Emodi* is distinguished from that obtained from *P. peltatum* by the following test. *Podophyllin* Resin 0.4 Gm., is mixed with Alcohol 60% 3 Cc. and N/1 Potassium Hydroxide 0.5 to 1 Cc. added. Gelatinisation occurs with *P. Emodi* only.—U.S.X. modified by D. B. Dott, Quarterly Jl. of Pharmacy, '28,266.

POTASSIUM.

Sources of Potash Salts.

Leucite. The lava from the volcanoes extending from Naples to Rome contains leucitic deposits which are a source of Potassium, its presence being first established in 1796. Baron Blanc was the pioneer of its use on an industrial scale during the war. Pure Leucite contains about 21.5% Potash, 55% Silica and 23.5% Alumina, and has the great advantage of being readily attacked by weak acids, e.g. Citric, without formation of gelatinous Silica. The purest, found in Monte Santa Croce region contains only 0.5% Soda. Lava treated at works at Roccamonfina contains 3 to 10% Leucite, there being sufficient Potash available in this area to supply the world for 1,000 years.—C.D., Feb. 9, '24,184.

The Dead Sea. A quarter of the contents is solid matter. It contains 30 billions of tons of mixed salts, of which about 10 billion tons are common salt. The remainder is Potassium Chloride, Magnesium Bromide and other chemicals. With 1½ billion tons of Potassium Chloride, Palestine is the richest country in the world for Potash resources. To be worked up under rights from the Crown Agents for the Colonies.—*Daily Mail*, May 30, 1925.

Alcoholic Solution of Potassium Hydroxide Solution for analytical work.

B.P. '14 Appendix. 10% in Alcohol 90%.

Potassii Bromidum.

Solubility found to be 72.56 Gm. in 100 Gm. of water. The solubility is increased by the addition of Bromine.—A. F. Joseph, J.C.S. Apl. '20, p. 377.

DETERMINATION OF CHLORIDE IN.—In the Silver Nitrate titration method it is more accurate to add excess of silver nitrate and determine excess with standard sulphocyanide solution than to use potassium chromate. It is, however, better to oxidise the hydrobromic acid in acid solution with an oxidising agent, e.g., ammonium persulphate or lead peroxide. The hydrochloric acid being unaffected by these can be titrated with silver nitrate solution.—Caspari.

The *B.P.* '14 figure on titration on the dry salt assuming that nothing else is present other than Potassium Chloride indicates 98% purity.

Potassium Bromide 0.5 Gm. requires 42.01 Cc. N/10 AgNO_3

Potassium Iodide	"	"	30.125	"	"
Ammonium Bromide	"	"	51.04	"	"
Sodium Bromide	"	"	48.58	"	"
Sodium Iodide	"	"	33.35	"	"
Ammonium Chloride	"	"	93.5	"	"
Sodium Chloride	"	"	85.53	"	"

As an example : if 0.5 Gm. Sodium Bromide dry required 49.07 Cc. N/10 AgNO_3 the NaCl content would be $\frac{(49.07 - 48.58) 100}{85.53 - 48.58} = 1.4\% \text{ NaCl}$.

—Based on some figures in Evans' Anal. Notes, 1914—1919. See also A. J. Jones, C.D. '19, 1150.

The determination of minute amounts of **Bromine in Saline Residues** and halogen mixtures by a modified Deniges Test. The Bromide is treated with KMnO_4 and H_3PO_4 at 85—90°, and the liberated halogen is aspirated into a decolorised Fuchsin solution. The colour obtained, on shaking with Chloroform, is compared with controls.—A. J. Jones, P.J. i./12, 475.

Fr. Cx. Supp. had the following test for **Chlorides**, but it is not in *Nouv. Supp.*, 1926.

Distill 5 Cc. of 10% Potassium Bromide solution with 50% sulphuric acid and 10 Cc. of saturated Potassium Permanganate Solution into a cooled tube containing 10 Cc. of the following :—Saturated Aniline Water 100 Cc. Water saturated with ortho-Toluidine 20 Cc. Acetic Acid (98%) 30 Cc.

If the salt contains much Chloride the liquid will assume first a blue and then violet-red colour. The latter should not occur in the official salt, at least within 15 minutes.

Quantitative separation of the Halogens—A. S. Swinton, P.J. Dec. 25, 1897.

Determination of Iodine in a mixture of Haloids.—An amount corresponding to about 0.2 Gm. Iodine is dissolved in water 10 Cc., and Sulphuric Acid 5 Cc. added with cooling precautions. Add Phenol (90%) 5 Cc. and saturated Bromine Water 20 Cc. with agitation. Wash out the Iodine with Chloroform, wash again, and repeat the separation with Phenol and Bromine Water. Add water and titrate with N/10 Thio.

Determination of Bromides in the presence of Chlorides.—Dissolve 0.2 to 0.3 Gm. in water 10 Cc., add Sulphuric Acid (50%) 2 Cc. and Chloroform 20 Cc., then excess saturated Potassium Permanganate solution with shaking. Run the Chloroformic solution of Bromine into 20 Cc. Alcoholic solution of Potassium Iodide and wash again with Chloroform. Dilute well with water and titrate liberated Iodine with N/10 Thio.

Determination of Iodides, Bromides, and Chlorides in the presence of each other.—Dissolve 10 Gm. in water 250 Cc. and estimate the Iodide in 10 Cc. as described above.

Bromine Estimation.—Acidify 10 Cc. with Sulphuric Acid (50%) 2 Cc. Remove Iodine by adding theoretical quantity of N/2 Potassium Permanganate solution and wash out with Chloroform, running it into Alcoholic Potassium Iodide solution as above. Set free the Bromine with excess saturated solution Potassium Permanganate, wash with Chloroform, and run into the same Potassium Iodide solution. Dilute with water and titrate total Iodine liberated.

To calculate the amount of Bromine subtract the number of Ccs. N/10 Thio required for the Iodide in 10 Cc. from the number required for both Bromide and Iodide in 10 Cc.

Chlorine Estimation.—Titrate 10 Cc. with N/10 Silver Nitrate, using Potassium Chromate. Subtract number of Ccs. N/10 Silver Nitrate which would be required for the known quantity of Bromide and Iodide in 10 Cc. of the solution from the amount actually used in this titration. From the difference calculate the Chlorine present.

Potassii Percarbonas, $\text{K}_2\text{C}_2\text{O}_6 \cdot \text{H}_2\text{O} = 216.208$.

White crystals, soluble in water, giving off oxygen. Used chiefly as 'Anti-hypo' in photography, also for decolorising instead of Sulphuric Acid in Ziehl Neelsen's method of staining *Bacillus Tuberculosis*, *q.v.*

Potassii Cyanidum.

Potassium Cyanide $\frac{1}{2}$ grain made into a Pill with soap or other 'floating' material and colouring matter for tinting the water forms a good method of killing the larvæ of mosquitoes (*Culex pipiens*) in pools: 1 in 300,000 is said to kill in a few hours.—B.M.J. ii./11,712.

Potassii Chloras.

Schulze's Maceration Mixture.

A mixture of Potassium Chlorate 10 (moistened with water), with Nitric Acid 49; or a Solution of 0.06 Potassium Chlorate in Water 100 Cc. and 1 Cc. of Nitric Acid. For separation of muscle fibre in animal, and ligneous tissue in vegetable, histology. Distinguish from the following:—

Schulze's Chlor-Zinc-Iodine Reagent for Cellulose.

Dissolve 110 Gm. of Zinc in 300 Cc. of pure Hydrochloric Acid, and evaporate to 150 Cc. (Sp. Gr. about 1.8). Dissolve separately 12 Gm. Potassium Iodide in as little water as possible; add 0.15 Gm. Iodine. Mix the solutions, and filter if necessary, through asbestos.—Bower and Gwynne Vaughan.

Potassii Metabisulphis $K_2SO_3 \cdot SO_2 = 222.31$. FR. CX.

Anhydrous Crystals soluble in 2 parts of water. Treated with acid it liberates about 52 to 57% Sulphurous Anhydride. (FR. CX.).

Manufactured by passing Sulphurous Anhydride (SO_2) into Potassium Carbonate until saturated. The metabisulphite is then precipitated with Alcohol. This salt has a similar action to ordinary sulphite in preserving Pyrogallie Acid from oxidation and preventing the staining of gelatin films. On oxidation, free Sulphuric Acid is produced, requiring an extra amount of alkali to neutralise it.—(P.J.F., 1904). The Sodium Salt has analogous composition.

Potassii Permanganas.

In titrating Potassium Permanganate Solution containing Nitric Acid with Sodium Arsenite, the latter has a reducing value greatly in excess of that shown when no acid is present. A Manganic compound is probably formed.—Abst. Ann. Rep. Chem. Soc. 1919 (Vol. XV.), p. 135.

Potassii Tartras Acidus.

Cream of Tartar Substitutes.—These are usually Calcium Acid Phosphate. A sample examined by Evans was a mixture of Cream of Tartar with Sodium Acid Sulphate, but in such proportions that the whole of the Tartaric Acid would be liberated with the Cream of Tartar in solution, with an excess of about 10% $NaHSO_4$ still remaining. Another sample was a mixture of 'dry' Calcium Acid Phosphate and Sodium Chloride.

PRUNI VIRGINIANÆ CORTEX.

Identification of various Spurious Cherry Barks. *P. Avium* is paler; taste bitter and astringent. Almond odor scarcely perceptible. *P. Pennsylvanica*, red brown, taste scarcely bitter. *P. Virginiana*; the bitter almond flavour is more perceptible than in any except *P. Serotina*.—Holmes, P. J. i./09,192.

The bark yields 0.075% or more of its weight of HCN.

Examination of a species, said to be closely allied to *P. emarginata*. The constituents, amongst which is Prunetin, a dihydric phenol $C_{16}H_{12}O_6$, dissimilar from those in *P. serotina*—when this substitute for the genuine article differs in that when it is moistened with water there is no formation of Benzaldehyde and Hydrogen Cyanide as with the genuine bark.—P.J. ii./10,604.

Syrupus Pruni Virginianæ.

Hallaway found the B.P. '14 method extracts 35%, Cline's 50%, Beringer's (with Glycerin), about 70% of the hydrocyanic acid. Glycerin extracts Tannin. Cline's process—which consists in macerating the bark 2 to 4 hours at 60° C., then percolating, adding Glycerin to the percolate and finally dissolving the sugar, is thought best. This reduces the Tannin content and increases the HCN, the enzyme being more active at the higher temperature, but even in the strongest syrup the HCN strength is only 0.008 per cent., or roughly 1/13 the strength of Cherry-Laurel Water.—P.J. i./09,798.

QUINIDINE, QUININE and other CINCHONA ALKALOIDS.

Including recent work on Cinchona Febrifuge.

See also Vol. I., p. 719.

Synthesis of Quinine, work on. Quinicine (Quinotoxine) has been converted into Quinine. (When Quinine and Cinchonine are heated with dilute Acetic Acid they are converted respectively into Quinotoxine and Cinchotoxine). The reverse change has been accomplished.—Ann. Rep. Chem. Soc. 1919 (Vol. XV.), p. 113. See also Prof. Greenish, Vol. I., p. 725.

Excretion of Quinine in treatment. There is no appreciable difference between the bi-hydrochloride salt given *per os*, intramuscularly or intravenously or by the first two combined. There is further no great difference in excretion of acid hydrochloride or hydrochloride or hydrobromide or acid hydrobromide or sulphate if given orally.—M. Nierenstein, Bristol University, abst. C.D., '10,965. See also MacGilechrist's work, Vol. I., p. 746.

Demonstration of the advantage of using Hydrochloric Acid in Cinchona extractions. 1.5% of absolute Hydrochloric Acid for Yellow Bark, and 2.5—3.0% for Red Bark advocated for first maceration.—W. L. Scoville, Jl. A. Ph. A., Feb. '23/104, per P.J. 1/23,300.

C. Ledgeriana, approximate determination as used by the planters. Extract with Ether, using Slaked Lime and Sodium Hydroxide. Solve residue in Ether in N/HCl and titrate with N/NaOH, using litmus. Precipitate tartrates of Quinine and Cinchonidine, filter, wash, dry and weigh. Determine optical rotation α and calculate quantity of Quinine and Cinchonidine from Cammellin's table. To the filtrate from the tartrates add NaI solution to precipitate Quinidine, Cinchonine and Amorphous Alkaloids. Separate Quinidine with 94% Alcohol.—Y.B.P. '23,8.

Quinine in tablets. Estimation by E. T. (Ether and Titration) method.—S. G. Liversedge and F. W. Andrews, P.J. ii./22,92.

Test for Quinine in Urine.

As native patients may omit to take their Quinine, test the urine with a few drops of Mayer's Reagent: a white precipitate appears if Quinine is present. To distinguish from Albumin, heat the upper part of the test-tube—if caused by Albumin the cloud becomes more dense, but if by Quinine it disappears when the liquid boils.—Per Jl. Trop. Med., May 1/28,105.

Brom-Phenol-Blue is a good indicator for titrating neutral Quinine salts.—N. Evers, P.J. i./21,470.

Quinine, Hydrogenation of, by reduction in presence of Formic Acid, using a Platinum catalyst or by using Nickel Oxide.—J.S.C.I., 1921,40,446R, Y.B.P. 1922,1. Many hydrogenated alkaloids have properties widely different from the originals and in certain cases their toxicity is reduced. See also Morphine and Colchicine Hydrogenation.

Growth of pathogenic bacteria.—Experiments with blood and the effect of certain antiseptics, including quinine and iodine, on the growth of staphylococci and streptococci in the blood, showed that no growth takes place when no quinine is present, but in the presence of one part of quinine in 800 parts of blood copious growth takes place; with iodine, growth increases progressively on raising the concentration of iodine in the blood from 1 : 25,000 to 1 : 400.—Sir A. Wright, C.D., Mar. 17/24,698.

History and development of the Cinchona plant.—A good resumé was given in a paper communicated by Lt.-Col. A. T. Page (late I.M.S.) to the Royal Society of Tropical Medicine and Hygiene, London, Jan., 1925.

After reviewing the various factors which led to the cultivation of Cinchona in Java, Ceylon and India, attention was drawn to the trial in India, in 1873, of *Cinchona Febrifuge* (then a mixture of the total alkaloids of *C. succirubra*) and the report of the Surgeon-General of that year of its efficacy in malaria, its low price and its ease of manufacture. The high market price of Quinine naturally resulted in the planting of more *C. ledgeriana* trees, and so, in 1903, the composition of the febrifuge consisted of a mixture of the residual alkaloids, after extraction of Quinine, from the barks of *C. ledgeriana* and *C. succirubra*, with a certain amount of added Quinine, to make it similar to the original. In spite of this, the quantity manufactured rapidly declined, and with the advent of the war the demand exceeded the possible supply,

and the price naturally increased. This has resulted in the inability of the vast multitude of natives, who are in continuous residence in mosquito-infected districts, of procuring the necessary treatment, and for them, in the absence of conclusive proof that one alkaloid, or combination of alkaloids, is far superior to all others, the fittest product is the one which can be produced and distributed at the least possible cost and can be used with the least supervision. It seems, therefore, that although Quinine has been proved to be the fittest separated alkaloid, some supplementation of it is indicated. This could be achieved most easily and cheaply by reverting to the cultivation of *C. succirubra*, and the extraction of its total alkaloids to form again the original Cinchona Febrifuge.

A further paper, dealing with the **Clinical Aspects of the use of Cinchona and its alkaloids in malaria**, was read by Lt.-Col. Clayton Lane (late I.M.S.). The action of Quinine in combating the malarial parasite is accomplished, either directly by the Quinine, or by a metabolite formed by, or from, it; if the former, the greater its concentration in the blood, the better; if the latter, then the less detectable, the better. Although only a small quantity of Quinine is excreted as such, it disappears very rapidly from the blood, as shown by experiments of intravenous injection. Further experiments consisted in the incubation of parasites in a medium containing Quinine in a much greater concentration than it would occur therapeutically. The medium afterwards injected into paralytics produced malaria, thus suggesting that the alkaloid acts indirectly or through the medium of a metabolite.

Regarding the salt best suited for oral use, it is evident that, as practically **no Quinine is absorbed by the stomach**, whatever salt is given it will be **precipitated in the intestine as base**. If, however, it be a metabolite which is curative, the salt which most easily admits of intestinal metabolism should be given.

Tissue destruction is caused by accumulation of Quinine base.

The reasons for the greater difficulty in eradicating a chronic, as against a recent, infection, needed elucidation, as also the different results obtained by standard treatment in different seasons.

F. B. Howard deprecated unstandardised mixtures which could be easily adulterated as a **retrograde step**.

The ease with which necrosis is caused by injections could be obviated by employing **solutions of the alkaloidal base**, this being the only rational method, in view of the fact that **the base is inevitably precipitated by the alkaline serum**. Further work has been conducted on these lines, and readers are referred to details on *Mannitol Quinine*, Vol. I., p. 732.

In this connection, it is of interest to note that in June, 1917, Warrington Yorke and colleagues published a paper (*Annals of Trop. Med. and Parasitology*, Vol. II., p. 173), in which was given accounts of experiments on the injection of Quinine Base, 1 Gm., dissolved in Alcohol 90%, 1 Cc., diluted to 3 Cc. with Sesame Oil. This caused sloughing, but the therapeutic results in recent benign tertian malaria were in no way inferior to those obtained by the same workers in similar cases by the use of a solution of a very soluble salt.

Sir Leonard Rogers mentioned that he had frequently had better results from Cinchonine Bihydrochloride than from the corresponding Quinine salt.

Approximately 75% of the *Quinine added to blood can be recovered*, being practically equally distributed between the cells and the serum. Quinine is probably carried by *adsorption*.—O. S. Gibbs, *Jl. Pharm. & Exp. Therap.*, June, '28, 190.

Possible relations between Lupinine and the Cinchona alkaloids.—B.C.A., '28, A1144.

Quinine Bisulphate and Oxyquinoline Sulphate can be and are absorbed from the vaginal tract of experimental animals when instilled in aqueous solutions.—D. I. Macht, *Jl. Pharm. & Exp. Therap.*, Oct., '28, 145.

Quinidine, Mechanism of death from. Cat experiments showed that the M.L.D. of Quinidine Bisulphate is dependent on the speed of administration, e.g., 25 mg. per kilo is usually fatal in a single dose, but with a smaller dose given at 6, 12, or 24 minute intervals the total M.L.D. increased to 0.1 Gm. per kilo. Striking fall in blood pressure immediately following injection or non-lethal doses.—B. Gordon and Co-workers, *Jl. Clin. Invest.*, Aug. '25, pef *Jl. A.M.A.* ii./25, 1162.

'**Malarene.**' Prepared from the mother liquors from which Quinine has been crystallised. **Cinchona Ledgeriana** bark of the Govt. of India contains very little of alkaloids which constitute Malarene, but **Cinchona robusta** contains 30% of Malarene alkaloids. Efficacy of Malarene as a drug in the treatment of malaria, definitely established. Certain forms of malaria found to answer more readily to treatment with Malarene than with Quinine; it is much cheaper than Quinine. Not thought advisable to start plantations solely for production of Malarene unless medical opinion demands much larger quantities.—C.D., Dec. 20/24,876.

M.R.C. Report on action of Quinidine in auricular fibrillation. In searching for a drug that would produce a notable prolongation of the refractory period of the auricular muscle, atropine was first examined but the customary chemical doses were not able to produce a maximal reaction but larger doses had definite effect. *Von Frey's* statements re Quinidine confirmed. It certainly lengthens the refractory period.—B.M.J. i./23,111,112.

RHEI RADIX.

Rhubarb contains Emodin, Emodin Mono-methyl Ether, Rhein, also Aloe Emodin, Chrysanophanol (Chrysophanic Acid) and glucosides of these.—U.S.D., 1926. *Earlier Refs. in 18th Edn.*

Evaluation on Chrysophanic Acid content, the results not being absolute, but well adapted for comparative purposes.—A. Tschirch and P. Schmitz, Q.J.P., '29,463.

According to P.G.V. should yield 35% extract on macerating 24 hours, with a mixture of equal parts alcohol and water. This is not in P.G. VI.

POWDERED RHUBARB, Standards suggested.—12 per cent. of ash on the air-dried drug, and 35 per cent. of extractive.—E. T. Brewis and H. Deane, P.J. ii./13,146.

Physiological experiments on mice with Rhubarb Extracts, *made in vacuo*, showed same to be more effective.—P.J. i./24,6.

Pulvis Rhei Comp.—Methods of analysis.—J. F. Liversedge and Co-workers B.P.C., 1926, P.J. ii./26,144; C.D., ii./26,241.

SACCHARUM.

Cane Sugar may (in the absence of a polarimeter) be approximately estimated by heating 1 Gm. of the same in 50 Cc. of water, to which 10 drops of hydrochloric acid have been added, for half an hour on a water bath. The solution is then cooled and neutralised with soda and made up to 100 Cc. with water, and the **Invert Sugar** thus formed is estimated with Fehling's Solution, 1 Cc. of which is approximately equivalent to 0.005 Gm. of Invert Sugar, the calculation being on the basis that 360 of Invert Sugar represent 342 of Cane Sugar.

Lumps of *Pure Cane Sugar* rubbed together in the dark produce luminosity.

Estimation of Invert Sugar in Cane Sugar.

U.S.P.X. gives the following: Dissolve 20 Gm. Sucrose in enough Distilled Water to make 100 Cc.: filter if necessary. To 50 Cc. of the clear liquid add 50 Cc. alkaline Cupric Tartrate solution: heat mixture so that 4 minutes are required to bring it to boiling point and boil for 2 minutes. Add 100 Cc. cold recently boiled Distilled Water, and collect and weigh the Precipitated Cuprous Oxide as follows. Prepare a Gooch crucible with an asbestos layer. Wash asbestos with Distilled Water, followed successively by 10 Cc. Alcohol and 10 Cc. Ether, dry at 100° C. for 30 minutes and weigh crucible. Filter Precipitated Cuprous Oxide through crucible, wash residue on filter with hot Distilled Water, then with 10 Cc. Alcohol, and then with 10 Cc. Ether, and dry at 100° C. The weight of the Cuprous Oxide does not exceed 0.155 Gm., corresponding to not more than 0.5% of Invert Sugar.

Polarimeter.

U.S.X. requires the O.R. at 20° C. in a solution containing the equivalent of 26 Gm. of sugar (previously dried to a constant weight at 105° C.) in 100 Cc. of water and using a 200 mm. tube to be not less than + 65.9°.

Decomposition products of sugars as affected by various oxidising agents. Formic Acid, a very small quantity of acetaldehyde and apparently glycuronic acid formed.—L. ii./11,1418.

Invert Sugar Syrup.—A non-fermentable syrup with sugar content of 80% (26—45% Invert Sugar and 52—35% Cane Sugar, to replace B.P.

Syrup. It has a higher gravity, 1.4 against 1.33. Does not crystallise and retains brilliant appearance. Costs 50% more than ordinary Syrup, but contains 20% increase in Sugar content. The taste is sweeter and less cloying. It does not cake so readily. It contains Sucrose as well as Dextrose and Levulose.—W. A. Whatmough, C.D., i./27,281; Y.B.P., '27,424.

SAPONES.

(See also Vol. I., p. 760.)

The following is the approximate composition of Pharmaceutical Soaps.—W. H. M.—B. & C. D. ii./94,575.

Sapo Animalis, Curd Soap. Principally Sodium Stearate; made with Sodium Hydroxide and a purified animal fat consisting principally of Stearin:—Fatty Acids 60%, Combined Alkali 9%, Uncombined Mineral Matter 2%, Water 30%. Limit Test for Alkaline Hydroxide and Carbonate and free fatty acid are imposed for this and

Sapo Durus (Hard Soap). Principally Sodium Oleate. Manufactured with Sodium Hydroxide and Olive Oil:—Fatty Acids 60%, Combined Alkali 8%, Uncombined Mineral Matter 2%, Water 30%. It is soluble about 1 in 20 in water.

Sapo Medicatus, P.G.VI., Ph. Ned. V. (Full directions for making are given), and **Sapo Venetus** (Syn. *Savon de Venise*) are similar.

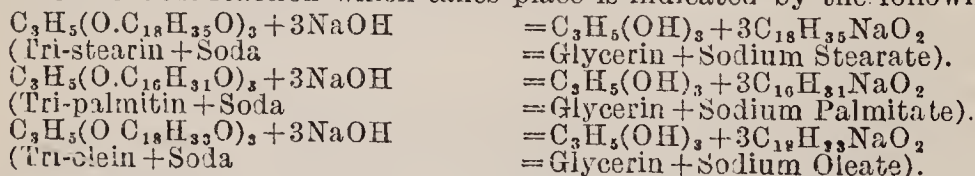
Castile Soap (Jabón Castilla).—By a Spanish Royal Order (Dec. 14, 1927) the name must apply only to a soap prepared in Spain, in the manufacture of which no fats other than Olive Oil have been used: containing not more than 2% Chlorides (as Sodium Chloride): maximum water content 25%: maximum free alkali content 0.3 Gm. per cent. The soap must be white and must be soluble in water or Alcohol without residue.—P.J. i./28,164.

Mottle is produced by adding iron or residues and scrapings of the lye tanks.

Sapo Mollis, Sapo Viridis, Soft Soap, consists principally of Potassium Oleate. Manufactured from Potassium Hydroxide and Olive Oil:—Fatty Acids 45%, Combined Alkali 8 to 11% (reckoned as K_2O), Insoluble Mineral Matter 1.0%, Water 35 to 45%, Matter insoluble in Alcohol 3% allowed (i.e. Potassium Carbonate and Insoluble Soaps).

In soap-boiling caustic soda of high purity, 96-98%, is used for the best varieties. The lye employed (into which the melted fat is poured) has Sp. Gr. 1.075. Boiling proceeds with occasional further addition of lye.

The chemical reaction which takes place is indicated by the following:—



The soap thus produced is salted out with salt, and the glycerin formed is recovered as much as possible from the spent liquor. It is essential to ensure that the fats have been thoroughly saponified, as also that no marked excess of alkali is introduced. The next step is to clarify the soap by boiling with a fresh supply of water from any insoluble soaps, e.g., Lime and Magnesium Salts of the acids indicated above. The "nigre" containing these impurities subsides in this manner to the bottom of the vessel. The soap is then allowed to slowly cool and "settle." When cooled to 165° F. it is removed to the frames to solidify. Here it remains for a month to consolidate and drain through apertures in the sides of the containing vessel before being cut up.

Potassium combined with saturated fatty acids, e.g. Palmitic and Stearic, yield hard soaps while the unsaturated acids, e.g. Oleic, yield soft soaps.

Marine Soaps are made from Coconut Oil and Palm Nut Oil. These oils contain, combined as glycerin esters, mainly lauric and myristic acids with some palmitic and oleic. They also contain Caproic, Caprylic, and Capric Acids. The presence of the three last mentioned is of importance because they render a soap made with coconut oil not easily salted out by sea water.—Prof. H. L. Smith, P.J. ii./15,33.

For Toilet Purposes special soap bases are employed containing a large

proportion of stearates (tallow). A proportion of palm oil is generally combined with the tallow. The soap ultimately is converted by machinery into ribbon-shaped shreds, it is perfumed and after other treatment is stamped in moulds. *Free alkali* is rarely present in appreciable amount.

For **Shaving Soap** it is necessary to employ fats—'strong' tallow—with a high melting point.

Pure Potassium Palmitate makes an excellent shaving soap, improved with a little glycerin. Sodium Palmitate and Sodium Stearate are not suited—they are not sufficiently soluble.—Prof. H. L. Smith, P.J. ii./15,33.

Shaving Paste with pearly lustre can be made with beef tallow and Potassium Hydroxide, replacing $\frac{1}{6}$ of the KOH with Sodium Hydroxide—*ibid.*

***Shavex** (T.M. 429,022).—A creamy preparation for shaving, having the advantage that no brush is requisite.

***Field Day** (T.M. 427,051) is also a preparation of this kind.

Household Soaps are made with vegetable oils of light gravity.

Good average soap can be produced by saponifying vegetable oils, such as Cottonseed, Palm, or Coconut (of this the best variety is known as "White Cochin" Oil, the second as "Ceylon" Oil); but these oils containing much of the Oleic Ester produce more soluble, *i.e.*, wasteful soaps.

The use of **Resin** in household soap is not injurious. It renders the soap smooth, prevents efflorescence, and cleansing 'odour' imparted is appreciated. Yellow bar soaps contain some 10 to 25%. Its chief *raison d'être* is probably cheapness. It is not, however, suitable for toilet purposes, and a large admixture cannot be allowed. Occasional additions to common soaps are chlorophyll, sodium silicate and French Chalk. **Sodium Silicate** has latterly come into use. Remarkable data are given by Prof. Smith—*ibid.*

Transparent Soaps are made by setting from methylated spirit. Many contain resin and sugar (as much as 20% of each). Only about $\frac{1}{2}$ the spirit is recovered—the rest is lost in drying. In Germany manufacturers may use pure spirit with 1 Kilo of Castor Oil and 400 Cc. of Soda Solution per 100 litres of Spirit to 'denature' it.

The **Valenta figure** records the temperature at which a mixture of equal volumes of Acetic Acid and Fatty Acid result in a uniformly clear and bright solution. The majority of the figures obtained and melting points, etc., approach those of Palm and Coconut Oils.—L. i./14,52.

Saponification Equivalents of Fats and Oils.

The **Saponification Number** or Köttstorfer's Number is the number of milligrammes of Caustic Potash which the fatty acids contained in 1 Gm. of the fat (free from moisture) are capable of neutralising. To 1.5 to 2.0 Gm. of the purified and filtered specimen for examination contained in an Erlenmeyer flask of about 200 Cc. capacity add 25 Cc. of N/2 Alcoholic Caustic Potash. Warm half an hour on water-bath with reflux condenser, with occasional rotation, add a little phenolphthalein solution and titrate excess of alkali with N/2 Hydrochloric Acid. Conduct a control using the alkali alone.

The difference in the number of Cc. of N/2 Hydrochloric Acid required to neutralise in the control and in the actual test is converted into the number of mgr. of KOH consumed by the amount of the fat or oil originally taken and the result is expressed in equivalent of 1 Gm. of the specimen.

Some Saponification Numbers :—

Adeps 195—203	Oleum Lini 187—195
Adeps Lanæ 90—102	Oleum Morrhuæ 179—192
Oleum Amygdalæ 191—200	Oleum Olivæ 191—195.
Oleum Arachis 190—196	Oleum Ricini 179—187
Oleum Chaulmoogræ 198—213	Oleum Sesame 189—193
Oleum Gossypii Seminis 191—196	Oleum Theobromatis 188—195.

A method of determining the **DETERGENT ACTION** of soaps depends on the quantity of Carbon which the Soap solution will carry through filter paper. The "**Carbon number**" is the number of grams carried by 1 Kg. of solution under standard conditions.—J. W. McBain and Co-workers, J. Soc. Chem. Ind., '23,42,373, per J.C.S., A ii./24,155.

Insecticides.

The power of a liquid to wet and spread over a surface is as important a factor as its toxicity to the organism against which it is directed. The addition of soap to a solution is useful as a "spreader."—Na., 114, '24,587.

For Iodine Number of Fats, see Iodum Chapter.

SCAMMONIÆ RESINA.

(See also Vol. I., p. 864.)

Scammony Resin is defined as a mixture of resins from Scammony root or from Orizaba Jalap root, *IPOMŒA RADIX*, B.P.'14. (*Ipomœa Orizabensis*), entirely soluble in Alcohol (90%). Not less than 75% soluble in ether. Tests are given for absence of certain foreign resins, especially Colophony.

In the testing of Scammony Resin for solubility in ether it is best to macerate 6 hours 3 to 4 Gm. of the resin finely powdered in 30—40 Cc. of ether in a short, wide-mouth flask. Filter off and weigh insoluble matter and give percentage on the dry resin.

The larger the quantity of Ether used the less Resin is dissolved. Digestion for at least forty-eight hours is necessary. The U.S.P. Ether, which has a Sp. Gr. of 0.713—0.716, gave a better yield than B.P. Ether.—H. Deane and W. E. Edmonton, P.J. i./21, 469.

Saponification Values characteristic of both the resins—of *C. Scammonia* 238 and *Ipomœa Orizabensis*—190—enables detection of the Mexican Scammony.—Am. Jl. Ph., Mar., '09, p. 105. See also P.J. i./12, 285.

SENNÆ FOLIA.

(See also Vol. I., p. 886.)

Senna Leaf Constituents.—An examination of Tinnevely leaves, leaves grown at Lima (botanically identical) and Alexandrian leaves, yielded (1) Salicylic Acid, (2) Rhein $C_{15}H_8O_6$, (3) Kæmpferol, (4) Aloe-Emodin and other bodies. The purgative action is in part due to the Aloe-Emodin—and other bodies.—F. Tutin, P.J. ii./13, 741; C.D. ii/13, 43.

Powdered Senna.—20 samples found free from actual adulteration, but some of them had been made from low-grade material, as shown by the absence of green colour and the presence of stalks and sand. Easy for the pharmacist to determine the quality of senna powder microscopically.—Prof. Greenish, P.J. i./13, 365, 370.

Senna and Gum Arabic. Account of French Government Expedition by Perrot & Alland in the Sudan with a view to acquiring knowledge for cultivation in the French African Colonies.—Prof. Greenish, P.J. ii./20, 488.

Ether shaken with a slightly acidified Senna Extract gives the Bornträger reaction—a pink or red colour with Ammonia water. If the Ether be shaken with a saturated solution of Nickel Acetate, the aqueous layer turns red, and if this be separated and Potassium Hydroxide added a violet precipitate forms, which is stated to be a characteristic test for Senna.—U.S.D., 1926.

SINAPIS SEMINA.

(See also Vol. I., p. 763.)

Black Mustard contains the glucoside Sinigrin, i.e.,

Potassium Myronate = $C_{10}H_{16}KNS_2O_8 = 397.36$, with Myrosin, which is similar to the ferment Emulsin in Bitter Almonds. This glucoside splits up under the influence of water with evolution of Allyl-iso-thio-cyanate, $C_3H_5NCS = 99.112$, the principal constituent of the Essential Oil, potassium acid sulphate and glucose. P.G. VI. requires Black Mustard Seeds to yield at least 0.7% of the allyl compound.

White Mustard Seeds (*Sinapis Alba*) do not yield Allyl Mustard Oil, but *p*-oxybenzyl Isothiocyanate, *Syn. Acrinyl Isothiocyanate*, $C_6H_4OH.CH_2O.NCS$. The Sinalbin contained in the seeds under the influence of Sinapisin and water decomposes forming that oil, Sinapin Acid Sulphate, and Glucose. The oil in question has a sharp taste. It decomposes on heating. It is insoluble in water, but readily in Alcohol or Ether. As the black seeds contain an excess of their glucoside and the white an excess of the ferment, the combination of the two produces the strongest effect. Some work by Prof. Greenish however (P.J. i./12, 203), shows that in all the samples of black mustard-seed examined—both old and new—there was sufficient myrosin to decompose all the sinigrin present, and that properly preserved black mustard-seeds retain their myrosin unimpaired for many years. Two samples examined contain sufficient myrosin to decompose a much larger quantity of sinigrin than the seeds themselves contained.

J. Gadamer has made a close study of these various constituents—see Schmidt, Pharm. Chem., Vol. II., Sections 1 and 2, for the latest views. The practice of adding Farina (wheat starch) to Mustard producing the fixed article 'CONDIMENT' MUSTARD is legalised by the 1875 Food and Drugs Act. The best table Mustard contains about 12 to 14%.—P.J. i./17,470. English Seeds from the Fen District and from Yorkshire considered the best. With one or two exceptions most manufacturers now retain the fixed Oil 'Condiment' Mustard.—*cf.* Vol. I., p. 763.

Oleum Sinapis Volatile.—The following tests are given *B.P.*'14.—Gr., 1.014 to 1.025. Distils between 148° and 156° C. Should contain less than 92% allyl-iso-thiocyanate, determined by *B.P.* process.

Essential Oil of Black Mustard (B.pt. 150.7° C.) is suitable for preserving wines, being 200 times as efficient as Sulphurous Acid, and not affecting colour, odour or taste of the wine. One Cc. of 1% solution per litre is usually sufficient. P.R. '24,84.

SODIUM.

Metallic Sodium has Sp. Gr. 0.973 and M. pt. 95.6° C. It boils at 742° C.

Electrolysed Brine used for hospital ship disinfection by means of a specially constructed cell (Mather & Platt) under Dakin's direction resulted in abolishing secondary infections among patients and ship's staffs and crews.—*ii.*/16,949.

Sodium, Ammonium and Potassium Persulphates are strong bleaching agents, the latter $K_2S_2O_8 = 270.32$, known as **Anthion**, and the Ammonium Salt are used in Photography to reduce dense negatives they oxidise and then dissolve part of the silver.

On adding Barium Chloride to a solution of Potassium Persulphate there is no precipitation, but on warming, Barium Sulphate is thrown down.

The Ammonium Salt $(NH_4)_2S_2O_8 = 228.208$ is prepared by electrolysis of a solution of ammonium sulphate containing sulphuric acid. In presence of water it yields ozonized oxygen. It bleaches, and has been used as a hand disinfectant. **To sterilise sponges.**

For details of the therapeutic use of the Sodium Salt, see Vol. I., p. 779.

Sodium Hyposulphite. See also Vol. I., p. 93.

To preserve volumetric Sodium Hyposulphite solutions a few drops of carbon disulphide added are useful.

Sodium Bromide (also Iodide) Solution for Pyelography, v. idem.

Sodium Acid Phosphate of commerce found to contain insufficient acid and too much water. A compound of the formula $NaH_2PO_4 \cdot H_2O$, requiring 3 Cc. N/1 NaOH to neutralise 1 Gm., and losing 10.5% at 105° C., can be made.—A. C. Abraham, P.J. i./25,54.

STROPHANTHUS.

(See also Vol. I., p. 789.)

Strophanthus Tincture, *B.P.*'14, is prepared by first removing the fat with Ether. U.S.X. employs Petroleum Benzine. The menstruum in the first case is 70% Alcohol, in the second 95%.

It has been stated that the fat in Strophanthus Tincture gives it an emetic action. Experiments on animals in America show this to be unfounded, the fat being void of action. On the other hand, a dose of fat-free tincture injected *subcutaneously* produced prompt emesis.

U.S.P., X., standardises biologically, as for Digitalis, *q.v.*

Six samples of Tincture of Strophanthus, *B.P.* assayed by the cat method, in terms of Ouabain supplied by the U.S. Dept. of Agriculture, were half the potency demanded by U.S.X. Ouabain of commerce is less toxic than that of the U.S. Dept. of Agriculture.—J. H. Burn, P.J., ii./26,439.

Ouabain in the assay of Tincture of Strophanthus. An average tincture would be equivalent to a solution containing 0.35% Ouabain or should not differ by more than 25%.—J. H. Burn, P.J., i./27,133,356. *The Ouabain method is now considered unsound.*

ASSAY BY CHEMICAL METHODS. HAYCOCK'S METHOD.

* The powdered seeds (20 Gm.) are freed from oil with Petroleum Ether and exhausted with Alcohol 70%. This tincture is evaporated at a low temperature, dissolved in 100 Cc. of Water, filtered, 3.2 Cc. of Sulphuric Acid (25%)

added, then shaken out thrice with 20 Cc. Ether. The aqueous acid solution is warmed for one hour at not exceeding 75° C. This decomposes the Strophanthin present into Strophanthidin and Strophanthobiose Methyl Ether. It is then cooled and shaken out with 10 Cc. of Chloroform. This is evaporated to a low bulk, allowed to crystallise out and dried below 65° C. The result divided by the factor 0.365 gives amount of Strophanthin present. Various samples of the seed by this method gave 3.1 to 4.57% Strophanthin. A standard of 0.1% w/v Strophanthin is suggested.—J. Haycock, P.J. i./11,553.

Fromme's 1910 Assay Method.

Consists in first extracting with Absolute Alcohol under a reflux, evaporating and defatting the extract. This is boiled with water and a few drops of Lead Acetate solution and then filtered, using Kieselguhr. The glucoside is next decomposed by heating with Hydrochloric Acid, and finally the Strophanthidin is thoroughly extracted with Chloroform and weighed. This multiplied by 2.187 gives the weight of Strophanthin represented. A similar process is used for the *Tincture*.—W. Kroseberg, P.J. i./14,590.

The poisonous property of the seeds is due to water-soluble glucosides. No active principle other than the water-soluble body was found. Methyl Alcohol is a good solvent. Chloroform is poor.—Karam Samaan, B.P. Conf., 1919.

Recommendation to substitute a preparation of **Strophanthin** in place of tincture of the seeds—unmixed Kombé seeds being now unobtainable in sufficient quantity. Suggestion that the seeds should be required to contain 6 to 8% Strophanthin and the Tincture 0.6%. Chemical assay in preference.—C.T. Bennett, B.P. Conf., 1920.

The geographical range of *S. Kombé* is limited. It might be well to order the use of *S. hispidus* instead—it is more easily obtained and is the only other species giving the green colour with Sulphuric Acid.—E. M. Holmes, P.J. i./19,33. *S. gratus* gives a rose colour.—Q.J.P., '28,439.

Recent specimens of *S. Kombé* are much mixed with *S. Courmontii*, whilst samples of *S. hispidus* can no longer be found unadulterated in commerce, and are entirely, or in large proportion, seeds of *S. sarmentosus*. A useful table gives the characters of Strophanthus species found in commercial samples.—F. J. Mathieson, per Q.J.P., '28,260,262.

Eight samples of Strophanthin tested by the Cat method, in comparison with U.S.X. Ouabain, gave an average potency of 47.3% of that of the Ouabain. Suggested that satisfactory Strophanthin should not vary from this average by more than 25%.—F. Wokes, Q.J.P., '28,516.

We are informed (June, 1929) that plenty of 100% Kombé Seeds are available, but their price is 50% higher than that for the unmixed variety.

Distinction between Strophanthin and Ouabain.

Strophanthin is soluble in water 1 in 40-43 at 15°. The aqueous solution of this glucoside, unlike that of Ouabain, gives a persistent froth on agitation.

The following distinguishing color test has been proposed: 5 Cc. concentrated hydrochloric acid, a few crystals of resorcinol and a trace of the glucoside are warmed to 60° or 70°. Ouabain gives no coloration, while strophanthin gives a rose color.—J.C.S. A. ii./21,601.

We tried this test and found it satisfactory.

Hispidus Strophanthin, like *Kombé* Strophanthin, is a mixture of two glucosides, but the structure of the latter is different in the two cases.—B.C.A., Dec., '28,1376.

TEREBINTHINA CANADENSIS.

The balsam obtained from *Abies balsamea* (*Coniferae*), known as Canada Balsam. Is a constituent of Collodium Flexile. (B.P. '14). It has a refractive index approximating that of microscopic glass, and 'sets' in a non-crystalline transparent condition, hence is used as a mounting medium. In preparing for use it has to be gently heated in an open dish for a week or more until a small quantity removed becomes brittle when placed on a cold slab. Canada Balsam 1 part by weight in Xylol, in turpentine, in benzol, and in chloroform each 1 by measure, are prepared for microscopic use. The first mentioned is chiefly employed and is frequently designated '**Xylol-Balsam**,'

Canada Balsam contains 18 to 20% of oil.

THEOBROMA.

(See also Vol. I., p. 804.)

Theobroma Oil, Detection of Adulteration.—An authentic specimen had following characters:—S.V. 196, I.V. 31, Volatile Fatty Acids 0.7%, Acid Value 0.6, M.Pt. 27° C. Butyrefractometer reading at 40° C. 46.5. Soluble in Ether 1 in 2, clear at 18°. Coconut fat, Bees Wax, Spermaceti, Vegetable Oils and Paraffin wax must be searched for.

W. Blyth and H. E. Cox (Foods: Their Composition and Analysis, 1927), give the following constants: Sp. Gr. at 15° C. 0.95 to 0.96, M.pt. 28°–32°, Saponification Value 193–195, Iodine Value 32–38. The Acid Value is 1.0 to 2.3, though the absolutely fresh butter should only require 0.06 to 0.22 Cc. N/10 alkali. It consists chiefly of the glycerides of Stearic, Palmitic, and Lauric Acids with small quantities of Linoleic, Arachidic, Formic, Acetic and Butyric Acids.

'Cocoa.'—The ground nibs of Theobroma Cacao from which most of the fat has been removed.

Cocoa is sometimes treated with an **alkali or an alkaline salt**, such as Potassium Carbonate, to render it "soluble," the alkali probably producing a more perfect emulsion of the fat.

Before and after treatment with alkali, Cocoa shows essentially the same lack of solubility, and hence the designation "soluble cocoa" is misleading and deceptive. (U.S. Board of Food Inspection.)

In pure untreated cocoa, the ash should generally be below 5.5%, with an alkalinity not exceeding 3.75, while with cocoas treated with alkali the ash is often as high as 8.5%, with an alkalinity exceeding 6. (Azor Thurston, Pharmaceutical and Food Analysis, 1923.) Allen also states that an alkalinity of more than 7.5 is indicative of treatment, the alkalinity being the number of Cc. of N/10 acid necessary to neutralise the ash from 1 Gm. of sample.

A number of samples were examined (1925), and it was found that in several cases the **high ash and alkalinity was suggestive of use of alkali in their preparation.**

The %Ash varied from 2.8 to 7.5, the average being 5.7. The alkalinity varied from 3.5 to 11.0, the average No. of Cc. N/10 acid required to neutralise 1 Gm. being 7.5.

None of the samples contained added starch. When treated with water as directed, the samples with high alkalinity did not give a better suspension than the untreated samples.

The examination of a number of Cocoas in the market showed moisture to range from 3 to 8%, *Nitrogenous Matter* (N \times 6.3) 19% to 20%, *Fat* 26 to 31%, *Mineral Matter* 3.9 to 8.8%. *Theobromine* 1.7 to 2.0%.—L. i./05, 316.

Cocoa Red is an astringent matter found in Cocoa, which on saponification breaks up into Glucose, Tannin, Resin and a phlobaphene.

Chocolate and Cocoa, a Disparagement of.—When containing a considerable proportion of Theobromine, if taken in excess, has been thought to be harmful. Theobromine is said to be a poison, coarsening and degrading the brain by inhibiting growth. It was stated that Cocoa retards the absorption of the proteins and fats of the food, especially those forms of Cocoa in which the fat has been partially removed, while on the other hand Cocoa with a large percentage of oil delays gastric secretion and may give rise to dyspepsia. The detrimental effects are, it was claimed, in the main due to the Theobromine. *Personally we should blame the fat.*

Neither by itself nor in combination with milk can cocoa be regarded as an important source of food protein.—B.C.A., '27, A170.

'Couvertures' is the Trade name for a good refined block chocolate, made by wholesale chocolate manufacturers for selling to makers of toffees, marzipan centres, etc., who do not make their own chocolate, but require it for dipping their sweets into. The Couverture is simply melted down and the sweets dipped.

Theobromine may conveniently be estimated by converting it into its **Periodide** $C_7H_5O_2N_4.HI.I$, and titrating the excess of Iodine. The process will work in presence of Sodium Acetate or Salicylate.—Abst. Ann. Rep. Chem. Soc. 1919 (Vol. XV.), p. 130.

New compounds of Caffeine and Theobromine (**Abelin**): Calcium Caffeine-o-acetoxy-benzoate and the analogous theophylline body.—J.C.S. A. i. 20, 327.

Ethyl-Theobromine is about twice as toxic as Caffeine, but is not diuretic in normal animals.—Y.B.P., '23, 356.

SUPPLEMENT.

Acidum Perchloricum HClO_4 . Available commercially 60% by weight with Sp. Gr. 1.54. A powerful acid and oxidising agent. May replace Sulphuric Acid in Kjeldahl estimations and in dehydration of Silica. For the former, *e.g.*, in estimating Nitrogen in milk, taking 10 Gm. of specimen, 4 Cc. HClO_4 (60%), 1 Gm. CuSO_4 and 25 Cc. H_2SO_4 , the time for digestion is reduced from $4\frac{1}{2}$ hours to 20 minutes. Similarly for blood (1 Gm.) 2 Cc. of HClO_4 is a useful addition to the H_2SO_4 and CuSO_4 .

It is to be noted there appears to be a limit to the quantity of HClO_4 used. A large amount results in a loss.

As a reagent for Potassium qualitatively and quantitatively has largely replaced the Chloroplatinate method.—B. Mears & R. E. Hussey.

Adsorption undoubtedly plays an important part in physiological processes. Examples are:—Adsorption power of charcoal towards Chlorine, Ammonia and Acetic Acid; of Colloidal Arsenious Sulphide towards Colloidal Hydrous Ferric Oxide, and probably enzyme action. Muscarine and Pilocarpine are inactive after they have actually entered the cells of the heart and intestinal muscle respectively. They are usually deposited on the surface of the cell and probably act from that position by adsorption. Strophanthin itself does not enter the cells of the frog's heart. It is allied to the saponins, which bodies have great effect in reducing surface tension.

Bassia Longifolia (see also Vol. I., p. 844). The seeds (Illipi Nuts) yield Illipi Butter (50%, it is stated), which is similar to Cacao Butter. It may generally be distinguished by absence of the typical odour of the latter. Sp. Gr. 0.857. Viscosity at 60° , 103.7 (against Theobroma Oil 99.9). M.pt. 33°C . Iodine Value 31.5. M.pt. of fatty acids 52.8°C . Saponification Value 190.

It is much used as a Chocolate Fat, but at the time of writing it is almost as high in price as Cacao Butter. The cake is poisonous and can only be used as manure. In commerce, Illipi Fat is however now a generic name for numerous articles—hence the above data may vary.

Refs.—Lewkowitsch, Chem. Technology & Analysis of Oils, Fats and Waxes, 1922. Tate & Pooley, Analyst, June, '21, 229.

Berberis aristata and other species. Histological study.—G. R. A. Short, B.P.C., 1926, C.D. ii./26, 262.

Berberine Sulphas.—Injections of 0.25 Gm. Berberine Sulphate in 1 Cc. Distilled Water said to be effective in oriental sore. Inject into the sore, and repeat after a week.—R. L. Varma, I.M.G., '27, 62, 84. This is insoluble, but $\frac{1}{4}$ grain Berberine Phosphate in 1 Cc. has been used.

Cadmium.—Instance of death due to fatty degeneration of the heart accelerated by the inhalation of Cadmium fumes.—P.J. i./23, 395.

Carbo Ligni.—A test for activity of medicinal and other Charcoals by exposure to water and other vapours. Active Charcoal will absorb 50 to 100%, or even more, of moisture. The water figure is slightly higher than that for Alcohol or Turpentine. *Pulv. Carbo. Lig.* as ordinarily dispensed for medicinal purposes is inactive. The author suggests improvements in the manufacture and the adoption in the B.P. of tests for activity.—H. Brindle, P.J. ii./28, 84; C.D. ii./28, 116.

Caryophylli Oleum.—Clove Oil from Islands of Pemba and Zanzibar—6% obtainable from the roots and 20% from the buds. The former contains higher percentage of Eugenol.—C. D., 1923, 98, 136.

Cedrus Atlantica. Distillation of Cedar sawdust in Morocco showed a content of 5% of oil, Sp. Gr. 0.9533, soluble 1 in Alcohol 90%.—Massy, P. R., 1922, 59. The wood yields 7% of tar.—Y.B.P., 1922, 59.

Costus Syn. Kunth, Kuth or Koot Root, Saussurea Lappa N. O. Compositæ. See also Vol. I., p. 852.

A liquid extract used for the treatment of asthma: 2 to 4 drachms stated to stop paroxysms. It may be taken as such in a little water (to cut short a paroxysm), or in the form of a mixture, taken 3 to 4 times daily, containing—Potassium Iodide or Potassium Bromide 5 to 10 gr., Tinet. Belladonna 3 to 5 m., Borax 2 gr., Liquid Extract of *S. lappa* $\frac{1}{2}$ to 2 dr., Spt. Chlorof. 10 m., Water 1 oz. (for continued administration). Has no emulative action. Is not claimed to produce a permanent cure.—R. N. Chopra, I.M.G., Apl., '28, 189.

Ephedrine is more prolonged in effect than Adrenalin. It is effectively absorbed when taken *per os* and is more stable. Valuable in hyperatrophic rhinitis and hay fever.—Chen & Schmidt, JI. A.M.A., Sept. 11/'26.

Nausea and vomiting likely if Adrenalin has been previously given. Some tolerance to drug in 15% of 39 cases. Further investigation necessary as to possible renal irritation—red blood cells and casts found in urine of several patients after short course.—L. i./28,144.

Ephedrine and Epinephrin both cause relaxation of the muscles of the chromatophores—the former being slow and more persistent.—P. J. i./28,353.

Low blood pressure.—1/8 to 1/4 grain produces very satisfactory rise in pressure and no toxic symptoms. 1/2 grain caused giddiness.—H. W. Hales, L. ii./28, 360. 4 mgr. Ephetonin equal to 2 mgr. Ephedrine.—F. R. Curtis, L. ii./28,226.

Whooping Cough.—Dose of 1/4 grain *per os* in watery solution to children of 1 year, and 1/8 grain for those younger, night and morning, of value. Most useful during second stage. No serious toxic symptoms.—B. M. J. E., 1./28,28.

A mixture of Ephedrine, Adrenalin and Potassium Sulphate produces local anæsthesia as intense as mixture containing Novocain in place of Ephedrine, though Ephedrine alone has no anæsthetic effect. Low toxicity. Suggested for use in dental surgery and ophthalmic work.—Per Pres., Apl., '28,132.

Adrenalin is 100 times more potent than Ephedrine Sulphate, but its toxicity is only 50 times that of Ephedrine injected hypodermically.—C. D. ii./27,818.

A synthetic substitute, Phenylethanolamine Sulphate (*Syn. α-phenyl-β-aminoethanol Sulphate*), of the formula $(C_6H_5.CHOH.CH_2NH_2)_2.H_2SO_4$, can be produced at about 1/10th the present cost of natural Ephedrine. It is pharmacologically similar but considerably less toxic. Clinically, it is inactive *per os* and has a weak pressor but also a weak bronchodilator effect hypodermically. Best used as a topical application in the nose, *e.g.*, in hay fever, in 2 or 3% solution, when its activity is in every way comparable to that of Ephedrine.—H. Miller and G. Piness, JI. A.M.A. ii./28,1035.

The pressor action of Ephedrine is reversed by Ergotamine.—F. R. Curtis, JI. Pharm. & Exp. Therap., Sept., '28,41.

Glucosides—Recent work on.—E. G. Bryant, P. J. i./28,213.

Glycyrrhiza. (*B.P.* '14) and *Glycyrrhizinum Ammoniatum*, U.S. IX.

The name 'Glycyrrhizin' applies to the sweet substance found in liquorice root, a mixture of Calcium and Potassium Glycyrrhizates.

Tschirch discovered that Glycyrrhizic Acid is the Diaglycuronic Acid ester of Glycyrrhetic Acid. It has glucosidal properties. Glycuronic Acid, of importance in animal life—an unexpected fact, as the most varied sugars are at the disposal of a plant if it wishes to form Glucosides.

A minimum of 9% of 'Glycyrrhizin' should be present in normally prepared edible juices—they should not contain more than 18% of sugars, reducing and non-reducing. In order to determine whether the starch be actual or added, the sample should be powdered, extracted with water and the residue taken up with 3% Ammonia Solution. The insoluble matter should never exceed 6%. Examine this under the microscope to trace source of starch, *i.e.*, whether added or of the same character as that in the root. The amount not dissolved in 70% alcohol should not exceed 16.5%. Gum should never be present in pure Liquorice Juice.—Parry, C. D. i./11,133.

The resins are confined to the bark of the root. With careful extraction with hot water these remain mostly in the marc.

Thirty-two samples of powdered liquorice examined. Three of the samples yielded less aqueous extract and nine exceeded the ash limit.—Professor H. G. Greenish and Dorothy J. Bartlett.—P. J. i./13,365,370.

B.P. '14 requires not less than 20% extract in the cold.

Glycyrrhizin—possible fatal dose 22 Gm., *i.e.*, 0.45 to 0.5 Gm. for a dog and 1.0 Gm. for a rabbit per kilo.—P. J. i./28,559.

Harmine (*v.* Vol. I, p. 861) and Banisterine (*v.* Vol. I, p. 845) identical: Harmine 0.04 Gm. hypodermically thrice daily useless in Parkinsonism; causes toxic symptoms.—T. R. Hill and C. Worster-Drought, L., ii/29, 647, 675.

Mesembryanthemum Edule Linn. grows on the cliffs near Dartmouth and has the power to lace the cliff-face together. It has been planted at Bournemouth in the angles in the crumbling sandstone and has spread over immense areas. The name should be altered to *Carpobrotus edulis* N.E.B. It is a native of Cape Colony. The fruits are eaten and known as Hottentot figs.

The juice of the plant has a reputation as a cure for dysentery and thrush and as an external application for burns. The fibrous roots bind sandy soil.—E. M. Holmes, P.J. i./28,468.

Nasturtium Officinale. Watercress, see Vol. I., p. 872. Vitamin 'A' in, see *Vitamins*, this Vol.

Niccolum.—Ni = 58.69. A constituent of German Silver:—Nickel 2, 3 or 4, Copper 8, Zinc 3½. The nickel coins in Germany consist of Copper 3, Nickel 1. **Bromide.**—NiBr₂ + 3H₂O = 272.57. *Dose.*—1 to 5 grains. Is in green deliquescent crystals soluble in water and in alcohol. To be given diluted. In epilepsy, 1 grain pills, action same as that of Potassium Bromide. **Sulphate.** NiSO₄·7H₂O = 280.866. *Dose.*—½ to 2 grains after meals. Greenish crystals, very soluble in water. Has been used in chlorosis (like iron augmenting number of blood corpuscles), amenorrhœa, splenic enlargement, and in locomotor ataxy. Resembles zinc sulphate in the fact that it is a nervine tonic and astringent. Allays nervous excitement and pain, particularly useful in cases where opiates cause vomiting, headache, and skin itching.

For Other Nickel Salts, *vide* Edn. XIV., p. 717.

Dimethyl-Glyoxime.—Delicacy of the test for Nickel.

Thorpe states 0.1 mgr. of Nickel can be detected in presence of 5,000 times as much cobalt, but gives no details as to the strength of solution. Our experiments using a 1% alkaline solution of Dimethyl-Glyoxime showed that:—

- 1 in 1,000 solution of Nickel sulphate gave copious pink precipitate.
- 1 in 10,000 " " " " " slight pink precipitate.
- 1 in 100,000 " " " " " pink colour precipitating after a time.
- 1 in 200,000 (= 1 in 1,000,000 Nickel) was the limit.

Further, Manganese alone gave no colour but in solution with an equal amount of nickel reduced the delicacy to about 1 in 2,000 of nickel sulphate. Cobalt chloride alone gave a brown colour but no precipitate. It also reduced the limit of delicacy to about 1 in 2,000 using equal parts cobalt chloride and nickel sulphate. See also A. C. Chapman, C.D. i./17,286.

Test for Nickel in Solution. Concentrated Ammonia Solution is added in excess to the solution containing Nickel; H₂S is passed through for a short time and the liquid then boiled. A bright mirror of metallic Nickel is deposited and the solution blackens. Cobalt does not interfere with the test.—C. G. Vernon, Chem. News, Mar. 29/23,200, per P.J. i./23,358.

Monel Metal.

An alloy of Nickel and Copper containing about 68% Nickel and a slight amount of Iron. Its strength approaches that of Steel and it has non-corrosive properties like Copper or Brass.—Thorpe, 1912.

Nicotiana Tobacum.

Tobacco smoking as an antiseptic idea thought to be a fallacy because it loads the blood with CO thereby wasting available Oxygen in the blood.—W. R. Meadows, P.J. ii./28,576.

Oleum Rosæ. Characters and Tests.—The Sp. Gr. of Otto ranges from about 0.850 to 0.860 at 30° C. (compared with water at 15° C.), R.I. at 25° about 1.460 to 1.465; M.Pt. about 20° to 22.5° C. Mixed with an equal volume of chloroform it does not congeal and is convenient for use. Saponification value (U.S. VIII) not less than 10 nor more than 17. It contains 70 to 75% of

Geraniol C₁₀H₁₈O = 154.144 (three-quarters of the liquid portion), and **Citronellol** C₁₀H₂₀O = 156.16 (the remaining 25%). Linalool is isomeric with Geraniol, Sp. Gr. 0.870. B.Pt. 197°. It is contained in Coriander, Thyme and other oils and is either + or — rotatory.

Geraniol is an important base in perfumery. It is not made synthetically, but occurs in a number of oils, especially Palmarosa and Java Citronella—in these it is free, in other oils it occurs as ester: Acetate and Tiglate.

'**Rhodinol**' is a blend of the two Alcohols Geraniol and Citronellol, from Pelargonium Leaf Oil. Some workers give the name as synonymous with Geraniol—others as synonymous with Citronellol.

75 or 76% at most is the highest amount of alcohol calculated as Geraniol that should be allowed in a normal pure Otto. Pure Otto never has specific gravity as high as 0.862. Frequently it is as low as 0.850. Any Otto with

a refractive index below 1.4600 is adulterated, and almost invariably with alcohol. Considering that about 50% of the adulterated samples contain alcohol, which is used to adjust the high Sp. Gr. and R.I. of the Geraniol Compounds added, the following test is valuable:—

If 5 Cc. be well shaken with 10 Cc. of warm water and the mixture allowed to separate, the refractive index of the washed oil at 25° C. should not differ from that of the original oil by more than 0.0015 (absence of alcohol).

The determination of the R.I. should be made on the separated otto when quite clear, filtered if necessary, but not dried with any drying agent, since the original oil, owing to the method of distillation is saturated with water.—Parry.

Though the predominating constituent, Geraniol is by no means the most important as both Citronellol and Nerol, and esters of the respective Alcohols and other bodies contribute largely to its fragrance. Phenyl Ethyl Alcohol, which possesses a mild odor, appears to be contained in Otto and in Nerol Oil, not only as such but also in form of esters of Benzoic and Phenyl Acetic Acids. Although this Alcohol is contained in exceedingly small quantity in Otto, it represents quantitatively the chief volatile constituent of rose petals. Being freely soluble in water, it remains behind for the most part in the aqueous portion of the distillate from which the Otto has been removed.

The so-called Stearoptene of Otto is a mixture of homologous hydrocarbons.

The presence of Otto in the air is readily recognised when only 0.000,000,000,000,000,333 Gm. of it is present in a cubic mm. of air.

Oleum Thymi. Phenols, determination of. With regard to the alkali used in the process a 5% Potassium Hydroxide is preferred. With Thyme Oil considerably higher results are obtained using 5 Cc. than with 10 Cc. of the Oil and about 100 Cc. alkali solution. Tests with Clove, Bay and Pimento showed it immaterial whether 5 or 10 Cc. of oil is used, but, with Cinnamon Leaf Oil a higher yield is shown with 5 Cc.—W. H. Simmons, P.R., 1921, 12,584, Y.B.P., 1922,80.

Italian *Thymus Vulgaris* Oil contained 38% Phenols, almost solely Thymol; 19% free alcohols in which Borneol and Linalool predominate probably; 18% Cymene and small quantity of Esters and free acids.—Leone and Angelescu, per Y.B.P., '22,85.

List of plants known to contain Thymol, includes *Carum copticum* 45 to 50%, *Thymus Zygis* 51%, *Ocimum gratissimum* 39.15%, *Origanum hirtum* var. *albiflor*, 51 to 60%.—Y.B.P., '23,119.

Thymol. Patents have been taken out for its synthesis starting from meta-Cresol and Cymene.—C.D., Aug. 25/23,296.

Originum Vulgaris Essential Oil from various parts of Italy. From Sicily the yield was 1.106% by distillation, and 2.38% by Acetone extraction. It contained 50% of Thymol.—Y.P.B., 1922,78.

Pectins occur in many fruits and vegetables, and are converted by means of the enzyme pectase, or by hydrolysis, into pectic acid, the calcium salt of which is insoluble and forms a jelly; the formation of jellies in fruit syrup is due to the production of calcium pectate. Pectin, on treatment with alkali, yields pectic acid, methyl alcohol and acetone. The methyl alcohol found in rum is attributed to the decomposition of the pectin of the sugar cane, and the methyl alcohol and acetone present in cider are derived from the pectin of the apple juice.—C.D.

Psoralea corylifolia (N.O. *Leguminosæ*). The seeds are in use in India as a remedy for skin diseases. The oil of this species is advocated for use in leucoderma (white leprosy).—J. C. Ghosh, P.J. ii./28,54.

Quinones.—Many Quinones, especially p-benzoquinone, found to be highly bactericidal, this power, however, being greatly reduced by the presence of organic matter (peptone, serum, urine), which seems to render them unsuitable as internal germicides.—G. T. Morgan and others, Jl. Soc. Chem. Ind., Dec. 12/24, per C.D. Dec. 27/24,915.

Rumex Acetosa, the Common Sorrel, found to contain 1.36% Potassium Binoxalate. *Oxalis Acetosella*, Wood Sorrel, contained 0.86%.—J. A. Purdie, C.D. i./27,127.

Scilla.—A manufacturer's Tinct. *Scillæ B.P.* found to be exceptionally strong physiologically, creating a dilemma for him.—C.D. i./27,287.

Selenium Organic Compounds.

(1) **Diamino-diseleno-benzene Hydrochloride.**— $\text{NH}_2\text{C}_6\text{H}_4\text{Se}.\text{SeC}_6\text{H}_4\text{NH}_2.2\text{HCl}$.
A brown amorphous powder easily soluble in water but slowly precipitating. Its analogy with Salvarsan makes it of interest but its instability is a disadvantage. This compound was made by G. T. Morgan.

(2) **Diseleno-phenyl-arsonic Acid.**— $\text{H}_2\text{O}_3\text{AsC}_6\text{H}_4\text{Se}.\text{SeC}_6\text{H}_4\text{AsO}_3\text{H}_2$.
A lemon coloured powder insoluble in water but soluble with the addition of one molecule of Sodium Hydrate.

We have had this tried pharmacologically in a 1% neutral solution, the result being that 0.12 Gm. per kilo intravenously killed a rabbit within 4 minutes, whilst a control of Salvarsan 0.1 Gm. per kilo was tolerated.

Attempts to form the Selenium analogue of Arsanilic Acid, namely **p-aminophenylselenic Acid** $\text{NH}_2\text{C}_6\text{H}_4\text{SeO}_3\text{H}$. Aniline Sulphate and Arsenate readily yield Sulphanilic Acid and Arsanilic Acid at an elevated temperature but no similar compound can be obtained from Aniline Selenate. *M-aminophenylselenic acid* and an acetyl and other compounds are, however, described.—F. L. Pyman, J.C.S., 1919, 166.

Senegæ Radix. Ext. Senegæ Liq.

Estimation by determining its Saponin content from its hæmolytic index. A 0.5% solution of the dried residue is made in a buffer solution of pH = 7.3, and a range of quantities from 0.1 to 1 Cc. of the solution added to tubes containing 1 Cc. of a 2% suspension of defibrinated human blood in Phosphate buffer mixture, all being made up to 2 Cc. The hæmolytic index is calculated from the tube where total hæmolysis occurs. The results of 7 examinations showed that the percentage of dried residue could vary from 8.8 to 28.6, with a corresponding variation of the hæmolytic index from 57 to 1,100.—P.J. ii./28,37.

***Staniform. (T.M. 479511 and 479512.) Methyl Stannic Iodide.**

Used in the form of powder or ointment in the local treatment of boils, ulcers, carbuncles, whitlows, acne, eczema, burns, chilblains, etc.

Tantalum. Ta = 181.5.

This element is usually classed chemically in a group with Vanadium (*q.v.*) and Niobium Nb = 93.1 as the Vanadium group. In some respects they are related to the Nitrogen group. They are trivalent and pentavalent. Tantalum is an extremely hard white metal; it is also malleable, ductile and elastic. It is unaffected by alkaline solutions or any acid except hydrofluoric. It is used in making electric light filaments, also for certain dental and surgical instruments. It can replace platinum for chemical processes which do not require high temperatures—above 600° C. it is oxidized so cannot be used for ignitions in chemical estimations.

Tantalite Ta_2O_5 (Mn. Fe) O is the only mineral worked commercially. It may contain as much as 84% Ta_2O_5 but rarely exceeds 70%. The process is secret but is probably a reduction with Sodium and fusion in vacuo.—Thorpe, Vol. 5, 1913, 399.

Telakucha (*Cephalandra indica*) has reputation in Bengal of remarkable effect in reducing amount of sugar in urine of diabetic patients. Fresh juice from leaves, stem and root found to produce no reduction of sugar in blood or urine in glycosuria.—R. N. Chopra and J. P. Bose, Ind. Jl. Med. Res., July, '25, per Jl. A.M.A. ii./25, 1432.

Tellurium Compounds, Organic.

The germicidal action of Cyclo-telluro-pentane-3-5-diones discussed. The 2-4 compound is readily soluble in water, and has been used successfully in cystitis and eye infections, and 2-6-dimethyl-c-telluro-pentane 3-5 dione is bactericidal in concentrations of 1 in 10,000,000 to 1 in 40,000,000.—G. T. Morgan and Co-workers, Jl. Chem. Soc. Ind., Oct. 3/24, 304, per C.D., Dec. 27/24, 914.

SPIROCHÆTICIDAL ACTION OF METALS.—Of 45 metals tested *in vivo* only 8 were found to be active spirochaetocides—Arsenic, Gold, Mercury, Bismuth, Vanadium, Ruthenium, Platinum and Tellurium. The last-named showed remarkable curative action, but a single dose gives strong garlic odour to breath persisting for months, and also causes blanching of hair and pigmentation of skin. Vanadium somewhat less active than Bismuth. Gold fairly active but has strong toxic action.—C. Levaditi, B.M.J. ii./28, 537.

Thallium Acetate—RINGWORM.—Thallium Acetate is distinctly inferior to X-rays in the hands of a skilled operator. Thallium often gives deceptive

appearance of cure, but fails to pass Woodd's Glass Test.—B.M.A. Ann. Meeting, J. E. M. Wigley, B.M.J. ii./28,307.

Death from 0.85 Gm. Dose should have been 0.85 centigram, *i.e.*, 0.0085 gm., in a teaspoon. The mixture was therefore 100 times too strong.—P.J. i./28,20.

It is a great mistake to introduce this strange division of the Gm. The best method of stating the amount in question would be 0.0085 Gm. or (not so good) 8½ mgr. Again the French, as frequently pointed out, write autologically, e.g. 0.05 cgr., meaning 0.05 Gm.

Distinctly inferior to X-Rays owing to the relative uncertainty with which it produces depilation, the slower fall of the infected hairs, and short time lapsing before recommencement of growth, the necessity for more skilled and vigorous local treatment during this time, the greater risk of reinfection of the growing hair owing to short time of baldness, the toxic effects, and the possibility of permanent serious damage to the growing organism.—J. E. M. Wigley, B.M.J. ii./28,984.

Therapeutic use of Thallium compounds **not justified**.—P.J. i./28, 603. Three deaths from—at Wembley—*ibid*, i./29,359.

After treatment the scalp is washed once daily. Tincture of Iodine 5% is applied twice weekly and Precipitated Sulphur Ointment rubbed in twice daily until complete regrowth of the hair is effected. The value of Sodium Thiosulphate in Thallium Acetate poisoning is not yet established.—per P.J. i./29,360; see also P.J. i./29,365.

ANIMAL ORGANOTHERAPY. PITUITARY GLAND.

Pituitary Extract.

The League of Nations Commission on the Standardisation of Serum, Serological Reactions and Biological Products recommended that the dry preparation of the Acetone-extracted fresh posterior lobe substance of ox-pituitary be now definitely adopted as the **International Standard** preparation for the biological evaluation of preparations of the posterior lobe of the pituitary, whether containing all the active principles of the lobe, or the pressor or oxytocic principle only, in separate solution.—B.M.J. ii./28,111. The standardisation of Pituitary Extract against Histamine is now recognised as unsound.—*ibid*.

PITUITARY IN LABOUR.—A dose of 2 units, if given before os is half dilated, hastens course of sluggish labour and is safe in any stage, providing there is no mechanical obstruction. Ampoules containing only 2 units should be available, as this dose appears safe at any stage.—A. W. Bourne and J. H. Burn, per B.M.J. i./28,273; P.J. i./28,125.

Investigation *re* dosage of Pituitary in labour.—J. H. Burn, P.J. i./27,133. Separation of the oxytocic and pressor principles of the posterior lobe (termed α and β Hypophamine respectively) as stable water-soluble powders.—B.C.A., '28,A554. See also H. W. Dudley, J1. Pharmacol, '23,21,103; P.J. ii./26,115.

Oxytocin *Syn.* ***Pitocin** (T.M. 496,396) possesses the typical stimulant action of Pituitary, whereas Vasopressin *Syn.* ***Pitressin** (T.M. 496,398) has no such effect, even in large doses. Oxytocin may safely be used in labour by those who have refrained from using Pituitary Extract, because of the danger of 'Pituitary shock.' It has the same action as Pituitary Extract, but is without any of its vasomotor effects.—A. W. Bourne and J. H. Burn, L. ii./28,695.

Each Cc. of 'Pitocin' contains 10 oxytocic units, and it is thus identical in activity with 'Pituitrin.'

'Pitressin' is used for the treatment and prevention of surgical shock, or the control of diabetes insipidus, and in cases of post-operative intestinal distension. Each Cc. contains 20 pressor units (one pressor unit being the pressor activity exhibited by 0.5 mgr. Standard Powdered Pituitary, U.S.P.). 'Pitressin' has thus double the pressor activity of 'Pituitrin.'

The action of the post-Pituitary principles (Oxytocin and Vasopressin) on the blood.—F. R. Curtis and J. W. Pickering, L., ii./28,695.

The mode of action of Pituitary on the parturient uterus may depend partly at least on the synergistic action of Oestrin.—A. W. Bourne and J. H. Burn, L., ii./28,1020.

Diabetes insipidus successfully treated by nasal administration of powdered Posterior Lobe. Used in the same way as snuff. Where polyuria varies between 15 and 20 litres in 24 hours, 15 to 20 cg. of powder are used daily, divided into 3 or 4 doses, where less than 10 litres from 5 to 10 cg. in 2 or 3 doses. The only contraindications are pathologic conditions of the nose.—Per J.L. A.M.A. ii./28,1411.

For further data on Pituitary, see Vol. I., p. 966; Histamine, Vol. I., pp. 406, 670, 673, 966.

SUPRARENAL CAPSULES.

Suprarenal Gland U.S., IX. (not in U.S., X.).—An assay process was provided by comparing the rise in blood pressure produced in a dog by an injection of an aqueous preparation of the gland with that produced by a dilute solution of Lævo-methyl-amine-ethanol-catechol.

EPINEPHRINE CONTENT, U.S. IX. TEST. (Requirement not less than 0.4 nor more than 0.6%.) Add 0.005 Gm. finely powdered Manganese Dioxide and 10 Cc. of water to 0.01 Gm. dry Suprarenal Gland. Thoroughly shake during 1 hour and filter. Compare the colour of the liquid in a test-tube with the colours produced by mixing a 2% solution of Cobaltous Chloride containing 1% concentrated Hydrochloric Acid and a dilute Gold Chloride solution (below). 1.85 Cc. Cobalt Solution + 0.95 Cc. of Dilute Gold Solution + 7.2 Cc. Distilled Water = 0.02% Epinephrine.

2.95 Cc. Cobalt + 1.25 Cc. Gold + 5.8 Cc. Water = 0.4% Epinephrine.

4.05 Cc. Cobalt + 1.35 Cc. Gold + 4.6 Cc. Water = 0.6% Epinephrine.

5.15 Cc. Cobalt + 1.55 Cc. Gold + 3.3 Cc. Water = 0.8% Epinephrine.

Dilute Gold Solution.—First make a strong Gold Chloride solution by dissolving 1 Gm. Gold Chloride ($\text{AuCl}_3\text{HCl} + 4 \text{H}_2\text{O}$) in 30 Cc. water.

Take 10 Cc. of this strong solution in a weighed porcelain crucible, add about 1 Cc. of 4% Ammonium Oxalate Solution and evaporate to dryness. Cautiously ignite until no further loss, and weigh. Calculate the exact amount of metallic gold in the solution assayed and dilute the remainder with water so that 100 Cc. contain 0.1 Gm. metal gold.

We have had some experience with this test and find it adequate. A sample of British Dry Suprarenal Gland showed 0.8% Epinephrine. A sample of American manufacture showed 0.4%.—W. H. M., Sept., 1920.

Mercurial Colorimetric Assay.

Macerate 1 Gm. of dry Suprarenal with 1 Cc. N/1 Sulphuric Acid and Distilled Water 5 Cc. for 15 minutes. Make up to 100 Cc. with Distilled Water and shake during 15 minutes. Filter. Dissolve Sodium Acetate 1 Gm. in water 8 Cc., and add exactly 2 Cc. of the filtrate, mix and add Mercuric Chloride solution 5% 3 drops. Mix. A bright red colour forms, reaching its maximum intensity in about 3 minutes. Compare with a standard solution containing Adrenalin 0.01 Gm., N/1 Sulphuric Acid 1 Cc., and Distilled Water to 100 Cc.—J.C.S., A. ii./25,248; P.J. i./25,660.

Other methods in earlier Edns.

Adrenalin.

TEST OF IDENTITY.—A peculiar odour like phosphoretted hydrogen is developed on treating a small quantity of the salt or solution with a few drops of sodium hydrate solution. See also Scheme for Recognition of Organic Chemicals.

Ewin's Colorimetric Test.—Potassium Persulphate is added to produce a concentration of 0.1% and the mixture placed in a boiling water bath. A red colour is produced. This shows Adrenalin in a dilution of 1 in 5 million.—H. Dryerre, C.D./22,418.

Urine, Adrenalin in.

Determined colorimetrically by the red colour produced on treating successively with Sulphanilic Acid, Nitrous Acid and Ammonia. Precipitate with Lead Acetate, and remove excess of Lead by Ammonium Sulphate. The determination is carried out on two portions, one of which has been treated with Ferric Chloride at 50° to destroy Adrenalin, the difference giving

Adrenalin content. By this method normal supplies were found to contain 0.2—0.4 mgr. per 100 Cc., larger variations occurring in pathological urines.—*J. Biol. Chem.*, '23, 57,497, *J.C.S.*, A. ii./24,75.

SODIUM HYPOSULPHITE prevents decoloration of Adrenalin solutions.—*P.J.* ii./24,204.

Mydriatic Power of Adrenalin. The eye of the frog is so sensitive to Adrenalin that it may be used to detect minimal amounts of the substance. May be used (instillation of the 1 in 1,000 solution) as diagnostic—though uncertain and inconstant. Functional disturbance of the pancreas, overaction of the thyroid, diabetes mellitus and perhaps exophthalmic goitre are associated with increased sensibility to Adrenalin. In all these states probably the adrenalin content of the blood is increased.—*B.M.J.* i./13,572.

Loewi's Test for Pancreatic Inefficiency.—2 or 3 drops of 1 in 1,000 Adrenalin solution dropped into the conjunctival sac and repeated after an interval of 5 minutes. In most cases no dilatation of the pupil occurs, but in a few there is conspicuous dilatation in $\frac{1}{2}$ or 1 hour. Loewi in Vienna found mydriasis only in one out of three cases of exophthalmic goitre and in 10 of 18 diabetics. Of undoubted value in the diagnosis of pancreatic lesions provided that its ways have been studied and its limitations recognised.—*Sir A. E. Garrod*, *L.* i./20,751.

Adrenine (Epinephrine) is present in the suprarenal glands of the whale, and can be separated from them, preserved in Chloroform after 6 to 9 months. Highest yield was 0.2% of the moist material, or about 1.2 Gm. from each gland.—*Y. B. P.*, 1913,2.

The relation between the concentration and the action of Adrenalin.—*D. Wilkie*, *Jl. Pharm. & Exp. Therap.*, Sept., '28,1.

Cortin, a potent substance removed from **Suprarenal Cortex** and free from Epinephrine. Keeps suprarenalectomised cats alive for an average of 27.4 days, as compared with 5 or 6 days with controls.—*Jl. A.M.A.* ii./28,1376.

The Adrenalin Test for Thyrotoxicosis.

Take pulse rate and systolic blood pressure of the patient (resting in bed) at short intervals until constant and a mean is obtained. Inject 0.5 Cc. Adrenalin Hydrochloride Solution 1 in 1,000 subcutaneously over the deltoid and take a further series of readings up till 15 minutes later, noting signs and symptoms. The test reveals the symptoms of incipient thyroidism, provides rough estimations of the degree of thyroid intoxication and the extent of reaction liable to follow operation. If reaction is absent or negative the goitre is not toxic, and there will be no post-operative reaction.—*Lambert Rogers*, *L.* ii./28,971.

Suprarenin (Synthetic). (*See also Vol. I., p. 977*).

A method of preparing a base having similar properties to Adrenalin was patented. English Patent (1912), No. 8957—now lapsed. The process is to reduce α -aminopropionylpyrocatechin with hydrogen in the presence of colloidal palladium and to separate the dextro- and lævo- compounds by means of dextro- and lævo- tartaric acids. The lævo- base has M.Pt. 218° C; the dextro-base melts at 217° C.

Hydroxy- and Dihydroxy-phenylserines and the parent substance of Adrenalin.—*J.C.S.A.i.*/20,56.

Patented Synthesis 118,298, by N. Nagai, see *J.C.S.A.i.*20,43;

Earlier Refs. to Patents—Edn. XVIII., p. 167.

Depressant action of Nicotine on Epinephrine output.—*Stewart & Rogoff*, *Jl. Pharm. & Exp. Therap.* June, 1919.

LIQUOR THYROIDEI.

Assay.—The author employs as standard 0.025 Gm. Iodine in organic combination in 100 Cc. of Liquor—this being based on an average content in the fresh gland of 0.04%, and the weight of the gland as at least 60 grains. The method of estimation is to determine the Iodine content in 10 Cc. of the Liquor on the lines of the process for *Thyroidesum Siccum*.—*q.v.*

As an example, we found fresh Thyroid glands to contain 0.063% Iodine. The Liquor made from them contained 0.015% Iodine. This indicated that

about 45% of the total Iodine had been extracted by the process. The Dry Thyroid from these glands contained 0.24% Iodine (1 of the Dry preparation was yielded by 3.82 of fresh gland). The average weight of the lobes of these glands was only 23½ grains. It would therefore seem desirable that the Liquor formula should be altered so that a specific volume should be made equivalent to *weight* of gland and be finally standardised to 0.025% organically combined Iodine.

Assay.

We advise as standard 0.2% Organic Iodine.

Dry Thyroid, 2 Gm., is mixed intimately with 2 Gm. of crushed Sodium Hydrate in a mortar. Heat in a porcelain crucible until of uniform grey colour. Cool and powder the ash in the mortar; and mix with 1 Gm. of powdered Potassium Nitrate; transfer to the crucible, heat over Bunsen flame until white or almost so (blowpipe not necessary). Dissolve the flux in 50 Cc. of Water and pour into a separator, add about 30 Cc. of Petroleum Ether, and then carefully sufficient 25% Sulphuric Acid in portions to render acid to litmus paper—shaking slightly so as to “catch” the Iodine in the solvent as liberated. After thorough shaking remove the aqueous layer and repeat the extraction with about 20 Cc. Petroleum Ether and a drop or two of 10% Sodium Nitrite Solution. Combine the Petroleum Ether Liquors, wash with water and titrate with N/500 Thiosulphate. (Note.—For 2 Gm. of a 0.2% preparation about 14 to 16 Cc. of Thiosulphate Solution will be required,—the addition of the Sodium Nitrite Solution is not really necessary).—*W. H. Martindale.*

Modified U.S.P. Process.—The faults found with Hunter's method as modified in the U.S.P., are loss of iodine on acidifying the solution of carbonates with phosphoric acid, and the introduction of oxychlorine compounds, including chloric acid, by the use of sodium hypochlorite solution. These compounds also liberate iodine from potassium iodide, and are not eliminated by boiling. With due care during neutralisation the first-mentioned source of error can be minimised, and where a fair proportion of iodine is present, error due to oxychlorine compounds is negligible.

The removal of chlorine by boiling after acidification should be controlled by starch-iodide paper until no reaction is obtained and the solution then boiled for a further fifteen minutes, instead of boiling for thirty minutes as directed. Where the iodine content is considerably less than 0.2 per cent., a modification of Kendall's method is best. One gram of the substance is gently heated with powdered caustic soda in a nickel crucible over an Argand burner. The crucible is heated more strongly until all the organic matter is oxidised, but no nitrate is added. The melt is extracted with water and filtered. Using Bromphenol-blue as indicator, the mixture is neutralised with phosphoric acid (Sp.gr. 1.75). Excess bromine water is added, and an excess of 2 Cc. phosphoric acid. The liquid is boiled to half its volume to expel bromine, the remaining traces being eliminated by adding salicylic acid after cooling. The iodine is liberated from the iodate by the addition of potassium iodide solution and the iodine titrated with N/200 thiosulphate.—Wilfred Smith, B.P. Conf., 1928; P.J. ii./28,88, Q. J.P. '28,372.

The iodine content in Thyroid Glands varies in different countries and at different seasons. We found in July, in one instance a content of 0.514% in the dry gland (equivalent to 0.1% Iodine in the fresh gland). On another occasion in March we found from the same source 0.24% Iodine in Dry Gland (equivalent to 0.063% in the fresh gland; 1 part of Dry Thyroid was = 3.82 of fresh gland). The weight of the lobes of these glands varied enormously—from 15 to 90 grains.

Further, we obtained thyroids from a number of English South Down Sheep slaughtered in January—these glands may be considered as a typical winter collection. The fresh substance yielded 25% Thyroideum Siccum

(i.e., 1=4 of fresh gland). On assay we found the dry gland to contain 0.368% Iodine equivalent to 0.092% Iodine in the fresh gland.

We recently found (**June, 1929**), that sheep's thyroids imported from the Argentine and closely trimmed, yielded 27% dried gland with an Iodine content of **0.378%**. The Iodine content in the fresh gland was evidently 0.102%.

According to an American authority,—

Thyroids Sheep's	may contain up to 0.04%	in the fresh gland.
„ Pigs'	0.0084 to 0.288%	ditto.
„ Ox	0.003 to 0.147%	ditto.
„ Human	0.006 to 0.08%	ditto.

Results in Europe with regard to sheep seem therefore to be better than in the U.S.A.

Temperature of Desiccation of Thyroid Gland.

P. NED V. requires 0.3% Iodine, and the temperature for drying is fixed at 30° C. Experiments have shown that if dried at 45° C. 70% of the Iodine becomes insoluble. *Sheep's Glands are specified.*

It should be noted that *B.P.*'14 requires the dry thyroid gland of the *sheep*, whereas U.S. X. allows 'domesticated animals which are used for food by man.' The **U.S. Product is not official in this country.** It is a much cheaper article.

Ox Thyroid Glands, Dry, contained 0.4187% Organic Iodine, according to our assay (W. H. M., Aug. 1920).

Sheep's glands desiccated yielded 0.06 to 0.28% Iodine and cattle 0.04 to 0.45%, while hogs' glands gave 0.17 to 0.47%; the latter, therefore, are the more fruitful. A statement as to the mass of confusion, commercial and in the matter of dose.—C.D., Sept. 23, 1922, p. 442. Any substitution of other animals' glands is a clear infringement of the *B.P.*'14 requirements.

Note.—The activity of the thyroid gland is attributed to Thyroxin. This is dealt with—Vol. I., p. 985. The percentage of Iodine may therefore be a measure of the activity of a thyroid preparation provided the glands have not been subjected to any treatment that would cause alteration in this substance.

Inorganic Iodine.—A test to exclude this is obviously necessary to prevent fraudulent dealing.

To detect addition of Iodine compounds, such as Iodised Albumin, mix 0.5 Gm. of sample with 1 Cc. of Ammonia solution and 9 Cc. 95% Alcohol. After 15 minutes, filter, and evaporate filtrate. Dissolve residue in small quantity of water, add a few drops of Chloroform and 10% Ferric Chloride solution. **Any violet colour indicates presence of Iodine in artificial combination, normal Thyroid Gland giving no colour.**—Fabre and Penane, *Jl. Pharm. and Chem.*, per C.D., Mar. 31/23, 438.

References.

It has been reported that thyroid feeding has very marked effect upon the synthesis of urea from ammonia in the liver. The tachycardia produced has been explained on the grounds of paralysis of the vagus, but later the thyroid protein bodies have been thought to directly injure the heart muscle. Individuals drinking from a so-called goitrous well show gross enlargement of the thyroid after a few weeks unless the water was boiled. A large number of patients develop Graves' disease immediately following severe emotional disturbance or nervous shock. These individuals of course carry a gland capable of reacting to this kind of stimulation, but it is certain that in 40% of the cases the stimulation occurred just before symptoms developed. "Developments in the Physiology and Pathology of the Thyroid Gland."—S. P. Beebe. "N.Y. Med. Jl.," 8/7/11.

Thyroid Gland, Seasonal Variation.—It has been stated that three times as much Iodine is found from *June to Nov.* as there is from *Dec. to May.* To obtain 0.2% Iodine one must mix the products of the high and low season of the year.

Our own experiments and those of Martin and others do not accord with this—at any rate on dry gland.

N. H. Martin, *P.J.* ii./12, 144, found as average in the dry gland from July to November, 1911, 0.36%, and in fresh gland 0.091%, and from December,

1911, to May, 1919, in dry 0.33%, and in fresh 0.086%. It is, however, more instructive to compare the content in the months of April to October inclusive with the Nov. to March figures on the fresh gland. The former are about double the latter owing to more moisture content in the winter. The Iodine yield from dry gland works out about the same throughout the year, viz., 0.34%.

Martin, in continuing his investigations, arrived at 0.25% as a fair Iodine Standard on examination of 13,927 lobes.—P.J., ii./13,123.

Glode Guyer made a prolonged investigation from December 12th to June 13th, on the weights of glands and moisture content. He found the ratio of dry to fresh gland as 1 to 3.6. The Iodine content on fat-free dry gland, through the period, supported our suggested standard of 0.2%.—P.J. ii./13, 123.

R. Bennett found 1 of dry powder = 4 of fresh substance. Martin found (1912) the yield to range from 1 = 2.58 to 1 = 5.66, i.e. an average of 1 = 3.39, subsequently (1913) the average was 1 = 4.15. Glode Guyer found in January, 1913, 1 = 3.34 and in June, 1913, 1 = 4.52. The question is raised as to how the old factor 1 = 5 arose.—P.J. ii./13, 804. Probably weight of fresh substance was taken on inadequately trimmed glands.—W. H. M.

Sheep in the Orkneys in winter consume seaweed, hence the iodine content in Dry Thyroid Gland may be 1.05%.—Jl. Biolog. Chem. per P.J. i./13, 625.

Iodine is a component part of the protein molecule of the thyroid gland but according to Herzfeld & Klinger it is not an essential constituent of thyroid secretion.—J.C.S.A.i./19, 608.

'Fresh gland basis' for thyroid is a survival of a non-scientific basis.—Duncan Flockhart and Co., L. i./21, 720.

Total storage capacity for Iodine of the normal thyroid said to be $\frac{1}{2}$ grain. It is therefore easy to keep the gland saturated.—Kimball, Med. Press, '23, 116, 4; Y.B.P., '23, 376.

Examination of Dried Glands of commerce. Sodium Fluoride and Boric Acid found. One (Corpeus Luteum) contained 63% Lactose.—Y.B.P., '23, 37.

The relation of the activity of the thyroid to the Iodine compounds occurring in the gland is not clear. The seasonal variation in the total Iodine of samples of Thyroid material from different parts of the U.S.A. was considerable—in Jan. and Feb. 100 lbs. of thyroid contained 14 Gm. of Iodine and in July and August as much as 40 Gm. This variation was not observed in material from England and Scotland. In the summer, when the Iodine content is highest, the percentage of total Iodine in the form of **Thyroxin** is not more than 10%, and in the winter less than 5%.—i.e. from 90 to 95% of the total Iodine is in some form other than Thyroxin. Chemical change can occur in Thyroxin not only when the glands are desiccated but when they are allowed to stand after being freshly ground. The Thyroxin is chemically altered and cannot be isolated, but it is still physiologically active. There appears to be another Iodine compound present in the gland which is destroyed with alkali, partly stable to acid, and has the physiological activity of Thyroxin. Thyroxin may be an intermediate form of the active constituent and it must be altered before it can become physiologically active—the alteration possibly being the attachment of a second hydroxyl group to the Thyroxin.—L.ii./28, 176.

Parathyroid Glands, Assay of.

The principle of the test is that if a preparation is incubated at 37° C. with a known weight of **Guanidine** in solution, the amount of Guanidine reckoned as guanidine picrate at the end of the incubation period is found to be less than at the beginning. Parathyroid is in some way able to prevent intoxication by Guanidine and its derivatives. Products vary in activity between 31 and 84—and, in the case of the desiccated powder, between 38 and 100—where 100 represents the maximum activity obtained with the powdered dry gland. Those tablets having an activity figure below 50 are probably valueless. In the process of manufacture, some activity appears to be lost, the relative value being: Whole Glands, 106, Desiccated Powder, 93, Finished Tablet, 76.—H. W. C. Vines, B.M.J., ii./23, 559. See also our Vol. I., p. 994.

Iodine content of parathyroid of no greater magnitude than that of ovaries, pituitary, or thymus.—per Jl. A.M.A. ii./25, 1428. It has been stated that it contains none.

PLACENTA.

The secretion of the Placenta has an inhibitory or controlling effect on thyroid, ovary and pituitary, thus explaining cessation of normal menstruation during pregnancy. Of value in treating menstrual disorders, also to threatened miscarriage due to over-activity of the post-pituitary, and assists in delaying onset of menstruation and in checking excessive bleeding. Relieves restlessness and irritability accompanying post-partum psychoses, e.g. mania and melancholia, and found of value in the severe occipital headaches of women, as also in some forms of migraine. Its action as a galactagogue is a matter of controversy.—per Pres., Oct. 23, 353.

Tablets each = 0.25 Gm. fresh substance stated to be effectual. Daily dose never exceeding 1.5 Gm.—B.M.J. i./17, 203.

Ratios Between Desiccated and Fresh Gland Products.

The American Drug Manufacturers' Association have agreed upon the following:—

Brain Substance	1—8	Pancreas Subs.	1—10	Spleen Subs.	1—5
Cardin ..	1—5	Parathyroid „	1—5	Suprarenal „	
Cerebrin	1—7	Parotid „	1—5	U.S.P. (stan-	
Corpus Luteum	1—5	Pineal „	1—6	dardised)	1—5
Duodenin	1—7	Pituitary		Suprarenal Cortex	1—5
Kidney ..	1—5	Whole Gl	1—5	„ Medulla	1—6
Liver ..	1—6	„ Anterior	1—5	Thymus (Calf)	1—6
Lymphatic Subs.	1—7	„ Posterior	1—6	Thyroid Subs.	
Mammary Subs.	1—8	Placental Subs.	1—6	U.S.P. (stan-	
Myelin „	1—9	Prostate	1—6	dardised in	
Orchitic „	1—7	Submaxillary Subs.	1—6	Iodine content)	1—5
Ovarian „	1—6	Spinal Cord „	1—9	P.J. i./28, 320.	

Hormones.

The most important **ductless glands** are the thyroid, parathyroid, pituitary and suprarenal. The cells of a gland have the power of forming one, or possibly more, hormones, each of which has the power of exciting a definite form of chemical activity in those cells for which it has a special affinity. The name **inhibitory hormones** (a contradictory one) is given to substances which, instead of activating, may control or inhibit chemical action.—G. R. Murray, L. ii./13, 201.

Hormones are thought to have the power to correlate and co-ordinate the various body functions (pregnancy, mammary secretions, etc.), but they also destroy toxins and may control one another—this is the “hormone balance.”

According to Bainbridge and Menzies, Hormones have a relatively small molecular weight, are easily diffusible, do not act as antigens and, in the case of hormones of the digestive tract, are not destroyed by boiling.

Pro-Secretin, the remarkable body found by Bayliss and Starling in the columnar epithelia of the small intestine, is an instance of internal secretion by a tissue, the main function of which is of a different nature. This substance when acted on by dilute acid yields **Secretin**, which after passing into and circulating with the blood provokes the secretion of the gastric juice and to a less extent that of the liver, it (Pro-secretin) exemplifies the class of hormones, bodies which give the character to internal secretions, and which, on absorption into the blood, influence tissues and organs other than those from which they have been obtained.

The testes and ovary, the intestinal epithelium, the pancreas, thyroid, the suprarenals and the pituitary body appear to yield specific hormones of physiological importance. It is held by some that the internal secretion of the ovary is produced by the corpus luteum.

Milk secretion is not the result of nerve excitation but is controlled by a hormone from the pituitary body.—E. A. Schäfer, Med. Press, March 19, 1913.

PHYSIOLOGICAL STANDARDISATION.

This method of testing is employed in those instances in which the drug contains no definite crystalline, easily isolated, active principle, e.g., an alkaloid capable of extraction.

It consists in "determination of the change in function induced in living organisms by the administration in the state of minute division of such inorganised substances as do not act merely as foods, for the purpose of identifying and adjusting the strength of drugs ; this may be either qualitative or quantitative."

The physiological action of a drug is the affinity it possesses for certain constituents of the cells of particular organs of the body. Thus Ergot has a specific action on the uterus. Cocaine has affinity for nerve endings, and Strychnine acts similarly on the spinal cord. Furthermore, as a result of the selective principle, drugs, according to their specific action on the organs, are designated stimulant, depressant, or irritant. The animals used for physiological determination should obviously be of the same species and weight, and should have been grown and kept under similar conditions. It is often useful to divide the small animals (e.g., frogs) into classes according to weight, and use these in 'batches' for experimental investigations. Much comparative work has been done with various **heart tonics**, e.g., Digitalis and Strophanthus (1) by direct application of a solution to the laid-bare frog's heart, and (2) injection intravenously or subcutaneously into dogs, rabbits, &c.

The quantitative test is based on the fact that the killing power of heart tonics for 'similar' frogs is constant per unit of body weight. Comparisons are made between effects produced by the sample preparation under examination and a standard preparation. e.g., a tincture made from genuine Kombé Strophanthus.

See further data under individual headings—Digitalis, Strophanthus, Ergot, etc.

The reaction between Acids and the Common Metals is a matter frequently arising and one concerning which information is not always available. In arranging the following table it was necessary to check many of the interactions experimentally as we found statements in the literature to vary greatly.

TABLES.

177

SUBSTANCE.	ACID HYDROCHLORIC.		ACID SULPHURIC.		ACID NITRIC.		REMARKS.
	Conc.* Sp. gr. 1.16.	Dilute.* Sp. gr. 1.048.	Conc.* Sp. gr. 1.841.	Dilute.* Sp. gr. 1.069.	Conc.* Sp. gr. 1.42.	Dilute.* Sp. gr. 1.057.	
† Aluminium Al ₂ O ₃	Hot.	Soluble. Forms AlCl ₃ .	Easily sol- uble.— Forms AlCl ₃ .	Slightly at- tacked. Forms Al ₂ (SO ₄) ₃	Soluble. Forms Al(NO ₃) ₃ and Oxides of Nitrogen.	Soluble. Forms oxides of Nitrogen.	Attacked by NaOH or KOH Solutions. Soluble in cold Acetic Acid, quicker in hot.
	Cold.	Ditto.	Ditto.	Unattacked	Slowly at- tacked.	Slowly attacked.	
	Hot	Slightly sol- uble. (Forms AlCl ₃).	Slowly sol- uble. (Forms AlCl ₃).	Soluble. Forms Al ₂ (SO ₄) ₃	Slowly sol- uble.	Slowly sol- uble.	
	Cold.	Almost in- soluble.	Ditto.	Ditto.	Forms Al (NO ₃) ₃ . Ditto.	Forms Al (NO ₃) ₃ Ditto.	<i>Ignited</i> (Amorphous) Oxide is unattacked by Acids, except hot H ₂ SO ₄ .
Antimony	Hot.	Pure Anti- mony is in- soluble.	Slightly sol- uble.	Insoluble.	Oxidised but not dissolved	No action.	Aqua Regia dissolves forming Antimon- ous or Antimonic Chloride according to duration of action.
	Cold.	No action.	No action.	Insoluble.	Practically no action.	No action.	
	Hot.	(Forms SbCl ₅).	Slightly sol- uble.	Slightly sol- uble.	Practically insoluble.	Very slight- ly soluble.	Soluble in KOH and NaOH Solutions. Insoluble in NH ₄ OH.
Antimonic Oxide. Sb ₂ O ₅ .	Cold.	Slowly sol- uble to form SbCl ₃ .	No action.	Slightly sol- uble.	Ditto.	No action.	

* = B.P. '14. † See also under Chromium.

SUBSTANCE.	ACID HYDROCHLORIC Conc.* Sp. gr. 1.16.	ACID SULPHURIC. Conc.* Sp. gr. 1.841.	ACID NITRIC. Conc.* Sp. gr. 1.42.	REMARKS.
Antimonious Oxide Sb_2O_3	Hot. Soluble. Forms $SbCl_3$ Soluble. Forms $SbOCl$ more or less according to proportion of Acid.	Soluble. Very slightly soluble.	Forms Sb_2O_5 Slightly sol- uble. and Sb_4O_6	Soluble in Acetic, Tartaric and Ben- zoic Acids, also in Glycerin.
Arsenium	Cold Slowly sol- uble.	Slightly sol- uble.	Slightly sol- uble.	Easily soluble in Aqua Regia form- ing $SbCl_3$ or $SbCl_5$ according to length of action.
	Hot. Slowly sol- uble Forms $AsCl_3$. Practically no action.	Soluble. Forms As_2O_3 and SO_2 . No action.	Soluble. Forms H_3AsO_4 Ditto.	Soluble in Sodium Hypochlorite Solu- tion.
	Cold. Practically no action.	No action.	No action.	
Arsenic Oxide As_2O_3	Hot. Soluble. Forms $AsCl_3$ and Chlor- ine on pro- longed boil- ing.	Soluble. Ditto.	Soluble	Very soluble in water.
Arsenious Oxide As_2O_3	Cold. Soluble with- out change.	Ditto.	Ditto.	
	Hot. Soluble. Forms $AsCl_3$. Forms more or less $AsOCl$ ac- cording to proportions of Acid.	Soluble. Slightly sol- uble.	Soluble. Forms H_3AsO_4	Soluble in Alkalies:
	Cold. Ditto;	Slowly sol- uble.	Ditto.	Slightly sol- uble, with- out changing

SUBSTANCE.	ACID HYDROCHLORIC. Conc.* Sp. gr. 1.16.	ACID SULPHURIC. Conc.* Sp. gr. 1.841.	ACID NITRIC. Conc.* Sp. gr. 1.42	REMARKS.
Bismuth	Hot. Scarcely acted on.	A slightly soluble basic Sulphate formed and SO ₂ .	Soluble. No action.	Aqua Regia converts into Bi Cl ₃ .
	Cold Insoluble.	Scarcely acted on. Schmidt says forms Bi ₂ (SO ₄) ₃ .	Soluble. Forms Bi (NO ₃) ₃ and oxides of Nitrogen.	
Bismuth Oxide Bi ₂ O ₃	Hot. Soluble. Forms BiCl ₃ .	Slightly soluble. Forms Bi ₂ (SO ₄) ₃ .	Soluble. Forms Bi (NO ₃) ₃ .	Soluble in strong hot NaOH Solution.
	Cold. Ditto.	Forms Bi ₂ (SO ₄) ₃ . Very slightly soluble. Easily soluble.	Ditto.	
Chromium (Reduced from CrCl ₃ by Zn.)	Hot. Soluble. Forms CrCl ₂ quickly oxidizing to CrCl ₃ .	Forms CrSO ₄ quickly oxidizing to Cr ₂ (SO ₄) ₃ .	Insoluble.	β, Chromium reduced from CrCl ₃ by ignition with Carbon is said to be unattacked by Aq. Regia or any Acids.
	Cold. Ditto.	No statement.	Practically no action.	
†Chromic Oxide Cr ₂ O ₃ (Green Amorphous.)	Hot. Soluble. Forms CrCl ₃ .	Forms Cr ₂ (SO ₄) ₃ .	Soluble. Forms Cr (NO ₃) ₃ (?).	Crystalline Cr ₂ O ₃ is insoluble in all Acids.
	Cold. Ditto.	Ditto.	Ditto.	

† NOTE.—By dissolving strongly heated Chromic Oxide in hot concentrated HNO₃ (1.4) a solution is obtained from which Cr₂(NO₃)₆.15H₂O crystallises on cooling. In dry air this loses 6H₂O with formation of Cr₂(NO₃)₆.9H₂O. Similarly Al₂(NO₃)₆.15H₂O is produced stable in ordinary air.—Milorad Z. Jovitschitsch Monatsh, 1912, 33, 9-18 per J.C.S.A. ii./12, 261.

SUBSTANCE.	ACID HYDROCHLORIC.		ACID SULPHURIC.		ACID NITRIC.		REMARKS.
	Conc.* Sp. gr. 1.16.	Dilute.* Sp. gr. 1.048.	Conc.* Sp. gr. 1.841.	Dilute.* Sp. gr. 1.069.	Conc.* Sp. gr. 1.42.	Dilute.* Sp. gr. 1.057.	
Chromic Oxide CrO_3 (Red)	Hot.	Soluble. Forms CrCl_3 and Chlorine.	Soluble. Forms $\text{Cr}_2(\text{SO}_4)_3$ and Oxygen.	Soluble with- out decom- position.	Soluble with- out decom- position.	Soluble with- out decom- position.	Very soluble in water to form H_2CrO_4 .
	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
Cobalt	Hot.	Soluble. Forms CoCl_2	Attacked. Forms $\text{Co}(\text{SO}_4)$ and SO_2 .	Soluble Forms $\text{Co}(\text{SO}_4)$.	Soluble. Forms $\text{Co}(\text{NO}_3)_2$ and Nitro- gen Oxides.	Soluble. Forms $\text{Co}(\text{NO}_3)_2$ and Oxides of Nitrogen.	
	Cold.	Ditto.	Unattacked.	Ditto.	Ditto.	Ditto.	
Cobalt (ous) Oxide	Hot.	Soluble. Forms CoCl_2	Soluble. Forms $\text{Co}(\text{SO}_4)$.	Not Attacked.	Soluble. Forms $\text{Co}(\text{NO}_3)_2$.	Soluble. Forms $\text{Co}(\text{NO}_3)_2$.	
	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	No Action.	
Copper	Hot	Very slowly soluble. Forms Cu_2Cl_2 (in con- tact with the air).	Slowly sol- uble. Forms CuSO_4 , CuS and SO_2 .	Not at- tacked.	Soluble. Forms $\text{Cu}(\text{NO}_3)_2$ and Oxides of Nitrogen.	Soluble. Forms $\text{Cu}(\text{NO}_3)_2$ and Oxides of Nitrogen.	Slowly soluble in Con- centrated Solutions of Caustic Alkalies.
	Cold.	Not attacked.	Not attacked.	Not attacked.	Ditto.	Scarcely attacked.	

SUBSTANCE.	ACID HYDROCHLORIC. Conc.* Dilute.* Sp. gr. 1.16. Sp. gr. 1.048.	ACID SULPHURIC. Conc.* Dilute.* Sp. gr. 1.841. Sp. gr. 1.069.	ACID NITRIC. Conc.* Dilute.* Sp. gr. 1.42. Sp. gr. 1.057	REMARKS.
Copper (sic) Oxide (Black) CuO	Hot. Soluble. Forms CuCl ₂ . Cold Ditto.	Soluble. Forms CuSO ₄ . Slightly sol- uble.	Soluble. Forms Cu(NO ₃) ₂ . Ditto.	Slowly soluble in hot concentrated caus- tic Alkali Solutions.
Copper (ous) Oxide (Red) Cu ₂ O.	Hot. Soluble. Forms Cu ₂ Cl ₂ . Cold. Forms Cu Cl ₂ and Copper.	Soluble. Forms CuSO ₄ and SO ₃ . Forms CuSO ₄ and Copper. Ditto.	Soluble. Forms Cu(NO ₃) ₂ and Cu(NO ₃) ₂ Oxides of and Oxides of Nitrogen. Ditto. Slightly soluble.	Same as Black Oxide;
Gold	Hot. Not attacked. Ditto. Cold. Slightly sol- uble.	Not attacked. Ditto. Slightly sol- uble.	Not attacked. Ditto. Slightly sol- uble.	Soluble in Aqua Regia to form AuCl ₃ .
Gold (ic) Oxide. Au ₂ O ₃ .	Hot. Slightly sol- uble. Cold. Ditto.	Slightly sol- uble. Ditto.	Soluble. Ditto.	Soluble in Conc. KOH Solution and KCN Solution.
Iron	Hot. Soluble. Forms FeCl ₃ . Cold. Ditto.	Soluble. Forms Fe SO ₄ and SO ₂ . No action.	Soluble. Forms Fe (NO ₃) ₃ and Oxides of Nitrogen. Ditto. Rendered passive.	Soluble. Forms Fe (NO ₃) ₃ and Oxides of Nitrogen. Ditto.

SUBSTANCE.	ACID HYDROCHLORIC.		ACID SULPHURIC.		ACID NITRIC.		REMARKS.
	Conc.* Sp. gr. 1.16.	Dilute.* Sp. gr. 1.048	Conc.* Sp. gr. 1.841.	Dilute.* Sp. gr. 1.069	Conc.* Sp. gr. 1.42	Dilute.* Sp. gr. 1.057.	
Iron (-ic) Oxide. Fe_2O_3 .	Hot.	Soluble. Forms Fe_2Cl_6 .	Soluble. Forms Fe_2SO_4 .	Very slight action.	Very slight action.	Practically no action.	Strongly ignited Oxide practically in- soluble in all acids.
	Cold.	Action slight.	Action practically nul.	Practically no action.	Practically no action.	Ditto.	
Lead.	Hot.	Action slight. Forms PbCl_2 .	Action very slight. Forms PbSO_4 .	Action very slight.	Action slow. Forms $\text{Pb}(\text{NO}_3)_2$ & oxides of Nitrogen.	Action vigorous. Forms $\text{Pb}(\text{NO}_3)_2$ & oxides of Nitrogen.	Action greatly depends on the condition of the lead—whether sheet or finely divided, etc.
	Cold.	Action very slight.	Action very slight.	Ditto.	Action slight.	Action slight.	
Lead Oxide (Litharge) PbO .	Hot.	Soluble. Forms PbCl_2 .	Soluble Forms PbSO_4 .	Forms PbSO_4 .	Readily soluble. Forms $\text{Pb}(\text{NO}_3)_2$.	Easily soluble. Forms $\text{Pb}(\text{NO}_3)_2$.	Soluble in conc. KOH and NaOH solutions. Easily in Acetic Acid.
	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
Magnesium	Hot.	Easily soluble. Forms MgCl_2 .	Easily soluble. Forms MgSO_4 .	Soluble. Forms MgSO_4 .	Soluble. Forms $\text{Mg}(\text{NO}_3)_2$.	Soluble. Forms $\text{Mg}(\text{NO}_3)_2$.	Soluble in Ammonium Chloride Solution.
	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
	Cold.	Ditto.	Ditto.	Action very slight.	Ditto.	Ditto.	

SUBSTANCE.	ACID HYDROCHLORIC. Conc.* Sp. gr. 1.16.	ACID SULPHURIC Conc.* Sp. gr. 1.841.	ACID NITRIC. Conc.* Sp. gr. 1.42.	REMARKS.
Magnesium Oxide. MgO.	Hot. Readily sol- uble. Forms MgCl ₂	Readily sol- uble. Forms MgSO ₄ & MgH ₂ (SO ₄) ₂	Readily sol- uble. Forms Mg(NO ₃) ₂	Soluble in Ammon- ium Salts, also in Organic Acids.
	Readily sol- uble. Forms MgCl ₂ .	Readily sol- uble. Forms MgSO ₄	Readily sol- uble. Forms Mg(NO ₃) ₂ .	
Manganese	Cold Ditto.	Ditto.	Ditto.	Ditto.
	Hot. Easily sol- uble. Forms MnCl ₂	Soluble. Forms Mn SO ₄ and SO ₂ .	Easily sol- uble. Forms Mn(NO ₃) ₂ & Oxides of Nitrogen. Ditto.	Easily sol- uble. Forms Mn(NO ₃) ₂ & Oxides of Nitrogen. Ditto.
	Cold. Ditto.	Action slight.	Ditto.	Ditto.
	Hot; Soluble. Forms MnCl ₂ and Chlorine.	Action slight. Forms MnSO ₄ and Oxygen at 200° C. for Mn ₂ (SO ₄) ₃ at 100° C.]. —Schmidt.	Action very slight. Forms : MnSO ₄ and Oxygen.	MnO ₂ is more sol- uble in diluted Sul- phuric Acid in presence of easily oxidisable bodies (FeSO ₄ , Sugar, etc.), with formation of MnSO ₄ and O, the O then oxidises the substances in question.
Cold. Ditto.	Action slight.	Practically no action.	No action;	
No action	No action;	No action;	Action very slight.	
No action	No action	No action	Action very slight.	

SUBSTANCE.	ACID HYDROCHLORIC. Conc.* Sp gr. 1.16.	ACID SULPHURIC. Conc.* Sp. gr. 1.841.	ACID NITRIC. Conc.* Sp. gr. 1.42.	REMARKS
Mercury				
	Hot. No action.	Forms HgSO_4SO_2 , and Hg_2SO_4 according to proportions and temperature. No action.	Soluble. Forms $\text{Hg}(\text{NO}_3)_2$ & Oxides of Nitrogen.	
	Cold Ditto.	Ditto.	Soluble. Forms $\text{Hg}(\text{NO}_3)_2$ & some $\text{Hg}_2(\text{NO}_3)_2$ and Oxides of Nitrogen	Very slightly soluble. Forms $\text{Hg}_2(\text{NO}_3)_2$
Mercury (-ic) Oxide Yellow or red variety HgO	Hot. Soluble. Forms HgCl_2 . Ditto.	Soluble. Forms HgSO_4 Ditto.	Soluble. Forms $\text{Hg}(\text{NO}_3)_2$ Ditto.	Combines easily with Organic Acids when freshly precipitated.
	Cold. Soluble. Forms NiCl_2 . Ditto.	Action slight. Forms NiSO_4 and SO_2 .	Easily soluble. Forms Ni Oxides of Nitrogen. Ditto.	
Nickel	Hot. Soluble. Forms NiCl_2 . Ditto.	Practically no action.	Soluble. Forms $\text{Ni}(\text{NO}_3)_2$. Ditto.	
	Cold. Ditto.	Ditto.	Soluble. Forms $\text{Ni}(\text{NO}_3)_2$. Ditto.	Soluble in NH_4OH
Nickel (-ous) Oxide NiO .	Hot Soluble. Forms NiCl_2 . Ditto.	Forms NiSO_4 . Ditto.	Soluble. Forms $\text{Ni}(\text{NO}_3)_2$. Ditto.	
	Cold. Ditto.	Ditto.	Soluble. Forms $\text{Ni}(\text{NO}_3)_2$. Ditto.	

SUBSTANCE.	ACID HYDROCHLORIC.		ACID SULPHURIC.		ACID NITRIC.		REMARKS.
	Conc.* Sp. gr. 1.16.	Dilute.* Sp. gr. 1.048.	Conc.* Sp. gr. 1.841.	Dilute.* Sp. gr. 1.069.	Conc.* Sp. gr. 1.42.	Dilute.* Sp. gr. 1.057.	
Nickel (-ic) Oxide Ni_2O_3	Hot.	Soluble. Forms Ni Cl_2 and Oxygen. Ditto. No action.	Soluble. Forms Ni SO_4 and Oxygen. Ditto. No action.	Soluble. Forms Ni $(\text{NO}_3)_2$ and Oxygen. Ditto. No action.	Soluble. Forms Ni $(\text{NO}_3)_2$ and Oxygen. Ditto. No action.	Soluble. Forms Ni $(\text{NO}_3)_2$ and Oxygen. Ditto. No action.	Soluble in NH_4OH c. evolution of Nitro- gen.
	Cold. Hot.	Ditto. No action.	Ditto. No action.	Ditto. No action.	Ditto. No action.	Ditto. No action.	Soluble in Aqua Regia to form PtCl_4 .
Platinum	Cold. Hot.	Ditto. Practically no action.	Ditto. Soluble. Forms Ag_2SO_4 and SO_2 .	Ditto. Action very slight.	Ditto. Soluble. Forms Ag NO_3 and Oxides of Nitrogen. Ditto.	Ditto. Soluble. Forms Ag NO_3 and Oxides of Nitrogen. Action slight.	Finely divided Sil- ver is more respon- sive than compact Silver to Hydro- chloric Acid.
	Cold.	Ditto	No action.	No action.	Ditto.	Ditto.	Soluble in NH_4OH KCN and Solutions.
Silver Oxide Ag_2O	Hot.	Forms AgCl	Soluble. Forms Ag_2SO_4 . Ditto.	Soluble. Forms Ag_2SO_4 . Slightly soluble.	Soluble. Forms AgNO_3 Ditto	Soluble. Forms AgNO_3 . Ditto.	Soluble in NH_4OH KCN and Solutions.
	Cold	Ditto.	Ditto.	Slightly soluble.	Ditto	Ditto.	Soluble in hot Con- centrated NaOH or KOH solution. Forms Stannates K_2 SnO_3 or Na_2SnO_3 .
Tin	Hot.	Soluble. Forms SnCl_2 .	Dissolves forming Sn SO_4 (Stan- nous Sul- phate) SO_2 and Sul- phur. Action slight.	Slowly sol- uble. Forms SnSO_4 .	Forms H_2 SnO_3 (Meta- stannic Acid) Ox- ides of Nit- rogen and NH_4NO_3 . Ditto.	Soluble. Forms H_2 SnO_3 , Sn $(\text{NO}_3)_4$ and Oxides of Nitrogen & NH_4NO_3 . Soluble. Forms $\text{Sn}(\text{NO}_3)_2$ NH_4NO_3 and very little gas.	Soluble in hot Con- centrated NaOH or KOH solution. Forms Stannates K_2 SnO_3 or Na_2SnO_3 .
	Cold.	Soluble. Forms SnCl_2 .	Action slight.	Practically no action.	Ditto.	Ditto.	Aqua Regia in excess dissolves to form Stannic Chloride SnCl_4 .

SUBSTANCE.	ACID HYDROCHLORIC		ACID SULPHURIC.		ACID NITRIC.		REMARKS
	Conc.* Sp. gr. 1.16.	Dilute.* Sp. gr. 1.048.	Conc.* Sp. gr. 1.841.	Dilute.* Sp. gr. 1.069.	Conc.* Sp. gr. 1.42.	Dilute.* Sp. gr. 1.057.	
Tin (-ic) Oxide SnO ₂ .	Hot.	No action.	Slightly soluble	No action.	No action.	No action.	Slightly soluble in hot conc. NaOH or KOH solutions.
	Cold.	Ditto.	No action.	Ditto.	Ditto.	Ditto.	
	Hot.	Soluble. Forms SnCl ₂ .	Forms SnSO ₄ . Soluble. Forms SnSO ₄ .	Soluble. Forms SnSO ₄ .	Forms SnO ₂ and Oxides of Nitro- gen. Ditto.	Forms SnO ₂ and Oxides of Nitro- gen. Soluble. Forms Sn(NO ₃) ₂ .	Newth says solution in NaOH is known as Sodium Stannite
	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
Zinc	Hot.	Soluble. Forms ZnCl ₂ .	Forms ZnSO ₄ & SO ₂ .	Soluble. Forms Zn SO ₄ and H. and if not sufficiently diluted H ₂ S. Soluble. Forms Zn SO ₄ and H	Soluble. Forms Zn (NO ₃) ₂ Ox- ides of Nit- rogen and NH ₄ NO ₃ .	Soluble. Forms Zn (NO ₃) ₂ Ox- ides of Nit- rogen and NH ₄ NO ₃ .	Soluble in hot Con- centrated KOH and NaOH Solutions.
	Cold.	Ditto.	Forms ZnSO ₄ .	Soluble. Forms Zn SO ₄ and H	Soluble	Soluble.	
	Hot.	Soluble. Forms ZnCl ₂ .	Slightly sol- uble. Forms ZnSO ₄ .	Soluble. Forms ZnSO ₄ .	Soluble. Forms Zn(NO ₃) ₂ .	Soluble. Forms Zn(NO ₃) ₂ .	Soluble in NH ₄ Cl. NaOH and KOH Solutions.
Zinc Oxide ZnO	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	

Spot Reactions on Paper.—It was found possible to test for all the members of the NH₄OH and NH₄HS group of Iron, Chromium, Aluminium, Nickel, Cobalt, Manganese, Zinc and Uranium Oxide, without any filtration, except when Cobalt and Zinc are both present.—Z. Anal. Chem., 1921, 60, 1; Y.B.P., '22, 133.

INDICATORS.

The following Indicators are those most generally used for Volumetric Analysis and for the Colorimetric Determination of the Hydrogen Ion Concentration of Solutions.

INDICATOR.	COLOUR CHANGE.	STRENGTH AND SOLVENT.	REMARKS.
Bromo-cresol Purple.	*PH 5.2 yellow. PH 6.8 purple.	0.04% in 20% alcohol.	"This is the most trustworthy indicator for Quinine."— <i>Jour. Amer. Chem. Soc.</i> , '22, 2156. Used for determination of the PH of solutions.
Bromophenol Blue.	PH 2.8 yellow. PH 4.6 purple.	0.04% in 20% alcohol.	Methyl Red, Methyl Orange or Cochineal give low results for Morphine, while Bromophenol Blue gives a satisfactory value and end-point. This is also true for Atropine and mydriatic residues.— <i>J.C.S., A.</i> ii./22, 885; also <i>P.J.</i> i./21, 470. Used for PH determinations.
Bromothymol Blue	PH 6 yellow. PH 7.6 blue.	0.04% in water	Used for colorimetric determination of PH of solutions.
Cochineal	PH 0—4 yellow PH 5 brown-pink. PH 6 lilac.	B.P. employs the <i>Off.</i> Tincture (1 in 10 Alcohol 45%.)	Useless for organic acids. Sharp end reaction with inorganic acids and bases by back titration. Suitable for solutions of the alkaline earths. Used for titrating alkaloids with mineral acids, but end reaction not sharp.
Congo Red	PH 3 blue. PH 4 violet. PH 5 scarlet.	0.5% in 25% Alcohol.	Responds well to inorganic acids and inorganic bases. Responds to organic bases, but not good for titrating, e.g. Quinine or Atropine.
Hæmatoxylin	Violet or purple with alkalis, yellow or orange with acids.	0.2% in Alcohol 90%. A few drops are <i>q.s.</i>	Responds to inorganic and to organic acids. Responds to inorganic bases, and to organic, e.g. alkaloids. Occasionally used in alkaloidal titrations, e.g. Quinine residues with good end reactions.

*PH 5 means a hydrogen ion concentration of 10^{-5} , see p. 190, when Bromo-cresol Purple is yellow. The addition of alkali to lower the hydron concentration to 10^{-7} changes the colour. Thus with acids this indicator is yellow and with alkalis purple.

THE EXTRA PHARMACOPŒIA.
INDICATORS—(Continued).

INDICATOR.	COLOUR CHANGE.	STRENGTH AND SOLVENT.	REMARKS.
Iodo-Eosin (Tetra-Iodo-Fluorescein).	Red with alkalis in aqueous solution, yellow with acids in ether layer.	0.1% in Alcohol. 0.01% in water. Sometimes 0.01% in ether is used.	Used for titrating minute quantities of alkali with N/100 or N/1000 acid and for small quantities of alkaloids which react alkaline to it. In use 10 to 20 Cc. of Ether is added to the titration flask to form a layer above the liquid. Alkalies produce a red in the aqueous layer and acids a yellow in the ether layer. It is a poor indicator, <i>e.g.</i> , with Strychnine. End point bad. —D. B. Dott, P.J.i./26,357. Not suitable for ordinary titrations.
Lacmoid.	PH 0—4 pink. PH 5 violet. PH 7 blue. These changes are not sharp.	0.2% in Alcohol 60%.	This indicator is somewhat less sensitive to CO ₂ than litmus, and is used similarly.
Litmus.	PH 4 red. PH 4.7 purple. PH 8 blue.	B.P.'14 Solution.	CO ₂ if present must be removed by boiling. Suitable for inorganic acids. Not suitable for weak acids and alkalies. Quinine, Morphine and Strychnine are neutral to it. The acid in their salts can be titrated, using Litmus as though no base were present. — P.J. i./15,135. But we find end points are not good.
Methyl Orange	PH 2.9 red. PH 4 orange. PH 5 yellow.	0.1% in water. A few drops are sufficient.	Suitable for titrating most inorganic acids but cannot be used for organic acids. Alkaloids are alkaline to, but end reaction not good, <i>e.g.</i> in case of Quinine. Alkali carbonates and bicarbonates can be titrated without boiling as this indicator is unaffected by CO ₂ . Do not use in alcoholic or boiling solutions. Acid Phosphates, <i>e.g.</i> Na H ₂ PO ₄ , are neutral to Methyl Orange.
Methyl Red	PH 5.7 red. PH 6.3 yellow.	0.2% in Alcohol. 0.02% in 50% Alcohol.	May replace Methyl Orange except when CO ₂ present, its end-points being sharper and it is far more sensitive in the titration of dilute solutions of weak bases.—U.S.P. Useful for cinchona residues and Strychnine. Used in determination of Hydrion concentration.

INDICATORS—(Continued).

INDICATOR.	COLOUR CHANGE.	STRENGTH AND SOLVENT.	REMARKS.
Naphthol Phthalein.	PH 7·3 colorless. PH 8·7 blue.	0·1% in Alcohol.	Used in determination of Hydriion concentration.
Phenolphthalein.	PH 8·4 colorless. PH 10 red.	0·5% in 60% Alcohol.	Usually employed for titrating inorganic and organic acids, and may be used in alcoholic or hot solutions. Some organic bases, <i>e.g.</i> the alkaloid Atropine, are alkaline to this indicator but Morphine, Quinine and Strychnine are not. Phenolphthalein must not be used in presence of ammonia or its salts, and is affected by CO_2 .
Phenolsulphonephthalein (Phenol Red).	PH 6·8 yellow. PH 8·4 magenta.	0·02% in water.	Used in determination of Hydrogen-ion concentration of solutions. It is employed in this way for blood and in media to differentiate typhoid and paratyphoid bacilli, <i>q.v.</i>
Potassium Chromate.	Red color due to formation of Silver Chromate which occurs only after haloid is all precipitated.	1 in 10 of water. A few drops of the solution are employed.	For titrating soluble haloids with Silver Nitrate. The solution of the haloid must be neutral as Silver Chromate is soluble in acid.
Potassium Ferrocyanide.	When blue or green coloration is no longer produced.	1% solution in water to be freshly made. Drops of it or a few small crystals are placed on a white tile.	Employed for titrating Ferrous Iron with Potassium Bichromate. Also used in titrating phosphate or arsenate with Uranium Acetate Solution. In this case the end point is the appearance of a brown color on the ferrocyanide crystal (after boiling the solution) due to formation of Uranium Ferrocyanide.
Rosolic Acid. <i>Syn.</i> Corallin, Aurin.	PH 6 yellow. PH 7 pink. PH 8 red.	0·5% in 50% Alcohol.	Responds to inorganic bases and to organic bases. Not suitable for use in presence of Ammonia or CO_2 . End-point not very sharp.
Starch.	Formation or disappearance of blue color.	0·5% in water, boiled and cooled.	For use in the titration of oxidisable substances, <i>e.g.</i> Arsenious Acid or Thio-sulphate, with Iodine or <i>vice versa</i> .

INDICATORS—(Continued).

INDICATOR.	COLOUR CHANGE.	STRENGTH AND SOLVENT.	REMARKS.
Thymol Blue.	PH 1.2 red. PH 2.8 orange. PH 8 greenish yellow. PH 9.6 blue.	0.04% in water	Used in determination of Hydrion concentration of solutions.
Thymol Phthalein.	PH 8 colorless. PH 10 blue.	0.04% in 60% Alcohol.	Used in determination of PH.
Turmeric.	Orange red with alkalis, yellow with acids.	Off. Tincture (1 Gm. with 6 Cc. Alcohol 90% by maceration).	Responds to inorganic and organic acids, also to inorganic and organic bases. Requires daylight. Not very satisfactory for alkalis, except Atropine. Suitable for estimating Boric Acid. Sensitive to Ammonia (1 in 35,000) and Potash (1 in 180,000).
Universal Indicator.	From PH 3 red in spectrum order of color changes to PH 11 reddish violet.		This mixed indicator is used for rapidly determining the approx. Hydrion concentration of a solution from the color obtained on adding 5 drops to 10 Cc. of solution. (See p. 191).

THE DETERMINATION OF THE HYDROGEN ION CONCENTRATION OF SOLUTIONS.

Theoretical Notes.

A solution is acid when it contains an excess of Hydrogen over Hydroxyl-ions, neutral when they are in equal numbers, alkaline when Hydroxyl-ions predominate, the product of the concentrations, $[H] \times [OH]^1$ in water being always constant at the same temperature ($10^{-14.14}$ at $18^\circ C.$).

An acid of "normal" strength contains in 1 litre 1 Gm. of Hydrogen capable of forming Hydrogen-ions and its strength may be viewed as 1 N. Pure water, however, dissociates to form Hydrogen- and Hydroxyl-ions and at $20^\circ C.$ contains approximately $1/10,000,000$ Gm. of Hydrogen-ions to the litre and an equivalent amount Hydroxyl-ions. That is to say, pure water, our standard of neutrality, is $1/10,000,000$ N acid and also $1/10,000,000$ N alkaline. For brevity this fraction may be expressed 10^{-7} N. Sorensen suggested dropping the 10 and the minus sign and calling it pH7. PH is therefore $-\log. [H]$. If there is less than $1/10,000,000$ Gm. of Hydrogen-ions in one litre, the solution is less acid than water, i.e. it is alkaline—so pH8 means $1/1,000,000$ N alkali and similarly PH 14 is $N/1$ alkali.

To conclude:

pH1 = $N/10$ acid.

•
•
•
•

pH6 = $N/1,000,000$ acid.

pH7 = NEUTRALITY.

pH8 = $N/1,000,000$ alkali.

•
•
pH14 = $N/1$ alkali.

The Use of Indicators.

For dark coloured solutions and for exact determinations of PH an electro-metric method is used but has the disadvantage of requiring complicated apparatus. However, for most practical purposes the colorimetric method, using indicators, is sufficiently accurate and is easily carried out. This process depends on the fact that every indicator changes colour over a definite zone of [H], suitable indicators being Thymol Blue, Bromphenol Blue, Methyl Red, Bromcresol Purple, Bromothymol Blue, Phenol Red, Thymol-phthalein.

The method consists in testing the solution with various indicators (5 drops to 10 Cc. of solution) until one is found which gives a tint lying between its extremes of colour. This gives an approximate value for the PH of the solution, and for more exact estimation the tint obtained is compared with that given by solutions of known PH and the same indicator until an exact match is observed. Details of suitable buffer solutions are given by N. Evers. (Analyst 1921, 393).

A Universal Indicator and Buffer Solution.

When the approximate PH of the solution only is required this can be rapidly ascertained by the use of a mixed or Universal Indicator which gives a series of colours at different values of PH. A Universal Indicator can be prepared by dissolving Methyl Orange 0.04 Gm., Methyl Red 0.02 Gm., Naphthol-phthalein 0.18 Gm. and Phenol-phthalein 0.08 Gm. in 100 Cc. of 70 % alcohol, and this gives the whole range of spectrum colours in the correct order from red (PH 3) to violet (PH 11). The hydrion concentration of a solution is found by adding 5 drops of this indicator to 10 Cc. and from the colour obtained the value of PH can be read off from the table below, but it is better to compare the tint with that given by solutions of known PH. For such solutions it is convenient to use the Universal Buffer Mixture proposed by E. B. R. Prideaux and A. T. Ward (J.C.S. '24, 426), which gives solutions of definite PH from 2 to 12 by neutralising with caustic soda solution. This solution contains H_3PO_4 1.961 Gm., Phenylacetic Acid 2.722 Gm., and Boric Acid 1.238 Gm. in 500 Cc. and for use 10 Cc. is mixed with the requisite amount of N/5 NaOH and made up to 20 Cc. The final solution is 0.02 N with respect to each hydrion, the whole being $n/10$.

The amount of neutralisation required for some PH values is shown in the table below, for intermediate values the graph in the original paper (*loc. cit.*) must be consulted. The formula $PH = 0.773 + 1.185 V$, where $V = \text{Cc. } n/5 \text{ NaOH per 10 Cc. of Solution}$, is sufficiently accurate for many purposes, and holds between $V = 1.5 \text{ Cc.}$ and $V = 9 \text{ Cc.}$

The colour changes of the Universal Indicator and the composition of the Universal Buffer Solution with different values of Hydrion Concentration.

APPROX. VALUE OF PH.	Cc. $n/5$ NaOH PER 10 Cc. BUF- FER SOLUTION in 20 Cc.	COLOUR WITH UNIVERSAL INDICATOR (5 DROPS PER 10 Cc.)	APPROX. VALUE OF PH.	Cc. $n/5$ NaOH PER 10 Cc. BUF- FER SOLUTION in 20 Cc.	COLOUR WITH UNIVERSAL INDICATOR 5 DROPS PER 10 Cc. SOLUTION).
2.0	0.0	—	7.5	5.6	yellowish-green.
3.0	2.0	crimson.	8.0	6.0	green.
4.0	2.8	red.	8.5	6.2	bluish-green.
5.0	3.6	orange-red.	9.0	7	greenish-blue.
5.5	4.0	orange.	9.5	7.3	blue.
6.0	4.5	orange yellow.	10.0	7.7	violet.
6.5	4.8	yellow.	11.0	8.5	reddish-violet.
7.0	5.2	greenish-yellow.	12.0	10.0	—

Bromophenol-blue—indicator corrections for temperature and presence of Alcohol.—J.C.S., A. ii./25,237.

Carbonate Titrations.—A mixture of Cresol Red and Thymol Blue gives a sharp end-point, corresponding approximately to the half-neutralisation point, and then the addition of Bromophenol Blue gives a sharp change from blue to green on complete neutralisation.—J.C.S., A. ii./24,627; P.J. i./25,8.

A mixture of equal parts of 1% Alcoholic solutions of Neutral Red and Phenol Red forms an indicator which shows a sharp change of colour at point of real neutrality, and is efficient for the titration of very weak acids and bases, but is sensitive to Carbon Dioxide.—J.C.S., A. ii./25,899.

A **Universal Indicator**, having a range from $\text{PH} 3.5-7.6$, and suitable for use in soil experiments, consists of a mixture of Alcoholic solutions of 0.04% Bromophenol-blue (4 vols.), 0.04% Bromocresol-purple (1 vol.), 0.02% Methyl Red (6 vols.), and 0.04% Bromothymol-blue (4 vols.).—J.C.S., A. i./25,348.

Chlorides may be titrated in neutral solution with Silver Nitrate, using 5 Cc. of 0.0125% Fluorescein as indicator, until a red colour is formed. For Bromides and Iodides, Eosin may be used.—J.C.S., A. i./24,60 and 776.

Chlorides may be titrated accurately in any acid solution using Potassium Chromate provided that the PH value is first reduced to between 5 and 7 by the addition of a Sodium Acetate-acetic Acid (2 mols : 1) buffer mixture.—J.C.S., A. ii./25,238.

Alkaloids.—In the titration of alkaloids by solution in excess of acid and back titration with alkali, the following indicators are recommended. They are based on the use of a solution containing 0.1 Gm. of the alkaloid in 50 Cc.

Methyl Red recommended for titration of Aconitine, Atropine, Brucine, Cephaline, Codeine, Cocaine, Diacetyl-Morphine, Emetine, Ethyl Morphine, Homatropine, Hyoscyamine, Morphine, Nicotine, Physostigmine, Strychnine, Thebaine and Yohimbine.

Bromocresol Purple for Cinchonine, Cinchonidine, Cotarnine, Ethyl Hydrocupreine, Quinine and Quinidine.

Bromophenol Blue for Delcosine, Narceine, Narcotine and Pilocarpine.—Analyst, '26,316; C.D., June 26/26,865.

Distilled Water, pH value of, obtained as $\text{pH} 6.7-6.6$, using dilute Methyl Red neutralised with Sodium Hydroxide colorimetrically.—B.C.A., Nov., '28,1203.

A buffer mixture of Succinic Acid and Borax for pH values 3.0-5.8, and of Succinic Acid and Potassium Hydrogen Phosphate for values of 5.8-9.2.—Jl. Biol. Chem., '25, p.135.

Hydrogen-ion control.—A useful summary.—It is pointed out that as the H-ion concentration of $\text{N}/10$ HCl is 0.0914 Gm. per litre and that of $\text{N}/10$ Acetic Acid 0.00136 Gm. per litre the HCl contains almost 70 times as many H-ions as the Acetic Acid.—W. A. Taylor, P.J. i./28,31.

A SCHEME FOR THE RECOGNITION OF ORGANIC CHEMICAL SUBSTANCES USED IN THERAPEUTICS.

The following scheme is intended to assist in the recognition of a number of organic chemicals, both natural and synthetic, used therapeutically. It frequently happens that the analyst is called upon to identify such substances, and without some guide the search is sometimes extremely difficult.

The Preliminary Tests are first carried out and, by comparison of the results with the tables, some idea of the nature of the substance may be obtained, enabling corroborative tests to be at once applied. If, however, no satisfactory evidence is obtained from the Preliminary Tests, it is determined whether the substance contains Nitrogen, Sulphur, Halogens or Phosphorus, a more complete

classification for the purposes of identification being based on the elements present.

Before commencing the analysis it should be ascertained, for example by treatment with solvents, whether the sample is one compound or a mixture, and if the latter a separation by chemical or physical means should be effected. No general rule for the isolation of the constituents can be given, but fractional distillation, crystallisation and solution methods are usually used, and extraction from an acid or alkaline aqueous solution with an immiscible solvent is often helpful when one component has basic or acidic properties.

PRELIMINARY TESTS.

1. The action of heat.

A small quantity of the substance is heated on a piece of foil or on the end of a penknife and the odour, behaviour, and presence of any inorganic residue is noted.

OBSERVATIONS.	COMPOUNDS.
ODOUR on heating :	Given by:—
(i.) Very objectionable	Acriflavin, Adalin, Anæsthesine, Eserine, Phenocoll, Yohimbin.
(ii.) Garlic-like. ..	Arsamin, Arrhenal, Chloralamide, Novarsenobenzol, Sod. Cacodyl., Sulphonal, Thiosinamine.
(iii.) " Burning sugar "	Citrates, Lactates, Tartrates, Sugars, Calcium Saccharate, Picrotoxin, Strophanthin, Glycerophosphates (very slight odour).
(iv.) Resembling pyridine (or " burnt feathers ").	The Purine Bases, Caffeine, etc., and their compounds.
(v.) Phenolic	Apomorphine, Amidopyrin, Morphine, Cinchona Alkaloids, Malachite Green, Phenazone, Stovaine, Strychnine.
	Inorganic Benzoates, Salicylates and Sulphocarbolates, Phenol compounds.
	Chinosol, Dimol, Tribromphenol.
	The characteristic odour of Salicylic Acid on heating is obtained with all its organic derivatives.
(vi.) Aromatic	Aconitine, Atropin, Cocaine, Colchicine, Hyoscin, Papaverine, Phenoquin, Sod. Cinnamate, Sod. Hippurate.
(vii.) " Sweetish " odour	Allantoin, Picrotoxin, Resorcin, Saccharin Ethylmorphine.
(viii.) " Alcoholic " ..	Chloretone, Homatropine, Sodium Veronal, Urethane.
(ix.) Amine Odour ..	Alypin, Apomorph., Betaine, Colchicine, Cryogenin, Ethylmorphine, Hexamine, Papaverine, Pilocarpine, Piperazine, Sod. Hippurate, Stovaine, Urea. Emetine Hydrochlor. (resembling Haddock).
(x.) Odour of burning animal or nitrogenous matter.	Albumin Tannate, Bile Salts, Argyrol, Dimol, Nuclein, Silver Proteinate, Eurobin.
(xi.) Pleasant Odour .	Sparteine Sulph. (Pea-like). Atropine (Nasturtium-like).

OBSERVATIONS.	COMPOUNDS.
APPEARANCE on heating :	
(i.) Low-melting solids (below 100° C.)	Acetophenone, Acids Oxalic and Stearic, Anæsthesine, Betol, Bromal Hydrate, Chloral Hydrate, Chloretone, Cocaine, Colchicine Salicyl., Coumarin, Guaiacol Benz. and Carb., Homatropin, Phenazone Salicyl., Physostigmine, Piperazine Tart., Salacetol, Salol, Thiosinamine, Thymol, Tribromphenol, Urethane.
(ii.) Coloured Fumes (a) of Iodine (b) Yellowish-brown	Alkaloidal Periodides, Emet. Bism. Iodide, Iodoform, Thymol Iodide, Tetraiodo pyrrol. Acriflavine, Chysarobin, Colchicine, Eurobin, Fluorescein.
(iii.) Incandescent Residue.	From Calcium and Magnesium Salts.
(iv.) Yellow Sparks	Acid Gallic, Alum. Aceto-Tart., Zinc Sulphocarb., Urea.
(v.) Boils and volatilises without appreciable charring.	Acids Acetyl-Salicylic, Malic, Oxalic and Succinic. Chloralamide, Cryogenin, Holocain, Naphthalene Tetrachlor., Phenazone, Piperazine, Propenal, Urea.

If an *inorganic residue* is obtained on ignition the substance is probably the metallic salt of an organic acid or phenol, and the following compounds, classified according to the metal present, are frequently employed therapeutically. In most cases tests for the acidic radicle, which can usually be separated as the sodium salt by treatment of the substance with alkali, are described later.

THE METAL PRESENT IN RESIDUE AFTER IGNITION	COMPOUNDS TO BE EXAMINED FOR:—
Aluminium	Aceto-Tartrate.
Antimony (with Sodium) ..	Sodium Antimony Tartrate.
(with Potassium) ..	Potassium Antimony Tartrate.
Bismuth (with Sodium or Potassium or both)	The Alkali Bismuthyl Tartrates. Benzoate, Citrate, Gallate, Oxyiodogallate, Naphthol, Tribromphenol, Salicylate, etc.
Calcium	Formate, Lactate, Acetyl-Salicylate, Glycerophosph., Saccharate, Guaiacol-Sulphonate. N.B.—Calcium and Sodium are found in the residues from Extracts and naturally occurring substances.
Iron	Ammon. Citrate, Tart., Oxalate, etc.
Magnesium	Glycerophosph., Peptonate, Valerianate. Acetyl-Salicylate, Borocit., Glycerophosph., Ricinoleate.
Manganese	Butyrate, Glycerophosph.
Potassium	Acetate, Oxalate, Borotart., Citrate, Formate, etc.
Silver	Colloidal, Argyrol, Proteinate, Nucleinate, etc.
Sodium	Indigo-Carmine. Mercurochrome, Novarsenobenzol, Veronal, Acetate, Formate, Glycerophosph., Salicylate, etc.
Zinc	Bile Salts. Oleate, Sulphocarbolate, Valerianate. N.B.—Zinc Salts are obtained on igniting some commercial dyes, e.g., Methylene Blue, Malachite Green.

2. The Action of Concentrated Sulphuric Acid.

About 0.2 Gm. of the substance is treated with 1 Cc. of Sulphuric Acid at first cold and then with heating.

OBSERVATIONS.	COMPOUNDS.
Cold Sulphuric Acid :—	
<i>Insoluble</i>	Saturated and aromatic hydrocarbons and their halogen derivatives :—Benzene, Xylol, etc.
<i>Effervescence—</i>	
(i.) HCl, HBr, HI.	From salts with organic bases, <i>e.g.</i> :— Alkaloidal Hydrochlorides, Acriflavine, Betaine Hydrochlor, Novocain, etc.
(ii.) Chlorine ..	Chloramine and Dichloramine T.
<i>Odour of Sulph. Dioxide</i>	Novarsenobenzol.
<i>Colouration—</i>	
(i.) Deep red ..	With certain glucosides, <i>e.g.</i> :— Salicin, Amygdalin, Arbutin. Aloes, Acriflavine, Iodinol, Proflavine, Phenolphthalein, Santalol.
(ii.) Light red ..	Nicotine, Physostigmine.
(iii.) Green	Methylene Blue. Strophanthin (changes to brown).
(iv.) Blue	Amyl Nitrite (changes to brown).
Hot Sulphuric Acid :	
<i>Effervescence—</i>	
(i.) Without charring	Acid Formic, Acid Oxalic, Betaine Hydrochlor., Urea.
(ii.) With blackening	Carbohydrates, some glucosides, Hydroxy-acids such as Citric, Tartaric, Lactic. Apiol, Malachite Green.
<i>Iodine Evolved</i>	Ethyl Iodide, Bismuth Oxyiodogallate, Emetine Bismuth Iodide, Thymol Iodide, Tetraiodopyrrol.
<i>Pungent Vapours—</i>	
Without Effervescence and Blackening.	Acids Acetic, Benzoic, Salicylic, Succinic, Acetyl-Salicylic, Phenols and metallic derivatives. Brometone, Chloretone, Chloral Hydrate.
<i>No Blackening</i>	Acids Carbolic, Benzoic, Salicylic, Acetyl-Salicylic, Meconic, and many of their compounds. Ethyl Bromide, Allantoin (red soln.), Alloxan (yellow soln.), Chloralamide (chloral odour), Alyphin, Fluorescein, Pyramidon, Purine Bases.

3. The Action of Alkali. Test solubility of substance in water, then add strong Caustic Potash solution and warm.

OBSERVATIONS.	COMPOUNDS.
Soluble in water ..	The following classes of common compounds are soluble :— Lower members of Monohydric, and also Di- and Trihydric Phenols. Lower members of Aliphatic Alcohols, Acids, Amines, Amides, Amino-Acids, Aldehydes, Acetone. Glucosides are fairly soluble. Carbohydrates, except starch and cellulose. Salts of organic acids or bases.
Caustic Potash with Heating :	
Substance dissolves ..	Acids, Amides, Phenols, some esters.
Precipitate forms ..	This may be hydroxide from metallic salt (which would be detected in Test 1). Organic Base from Salts (Morphine dissolves in excess KOH).
Odour of Ammonia ..	From Ammonium Salts, Amides, Ureides, Urea compounds, Chloralamide.
Odour of Amine ..	From salts, <i>e.g.</i> , Aniline Hydrochlor., Acetanilide, Exalgin.
Colouration—	
(i.) Deep red ..	Phenolphthalein.
(ii.) Yellow cold turning red on warming.	Many sugars.
Fluorescence	Fluorescein, Eosin.

4. Reaction for Alkaloids.

The solution should be tested for alkaloids by means of the usual reagents such as Mayer's Solution, Gold Chloride or Picric Acid. The table *postea*, may be useful in the identification of a common alkaloid.

In addition to the synthetic Cocaine substitutes the following bodies react in some cases like alkaloids :—

Bromethylformine, Chinosol, Phenazone, Phenocoll, Piperazine, Piperidine, Pyridine, Pyramidon, Quinoline, Thiosinamine, and some dyes such as Acriflavine.

The purine bases, Caffeine, Theobromine, Theophyllin, do not respond to many of the usual tests.

5. Reaction with Fehling's Solution.

It should be determined whether the substance reduces Fehling's before and after hydrolysis with dilute acid.

Substances readily reducing Fehling's Solution before hydrolysis.	Monosaccharides : Glucose, Lævulose, Mannose, etc. Disaccharides : Lactose, Maltose, etc. Fehling's is also reduced by some aldehydes, <i>e.g.</i> , Chloral, and polyhydric phenols, <i>e.g.</i> , Resorcin, Pyrogallie Acid, and by Chloroform, Chloralamide, Creatinin, Acid Camphoric, Cryogenin, Stovaine, Purine Bases.
Substances readily reducing Fehling's solution only after hydrolysis.	Disaccharides : Sucrose. Glucosides : Aesculin, Salicin, etc.

If sufficient data for identification have not been obtained from the above tests the compound should be examined for Nitrogen, Sulphur, Halogens and Phosphorus. Lassaigne's method is usually satisfactory, and consists in adding about 0.1 Gm. of the substance to a small piece of clean molten sodium in a test tube, and, after thorough heating, the mass is carefully treated with water.

Nitrogen.

A portion of the above solution is tested for cyanide by heating with Ferrous Sulphate, making acid with Hydrochloric Acid and adding one drop of Ferric Chloride Solution. A blue solution or precipitate of Prussian Blue indicates the presence of Nitrogen in the substance. Cyanamide, given by urea and derivatives, should also be tested for by means of Silver Nitrate, the silver salt being soluble in Nitric Acid but insoluble in Ammonia. Sodium Sulphocyanide may be formed if the substance contains Nitrogen and Sulphur.

Sulphur.

The formation of a deep violet colour on adding a small crystal of Sodium Nitroprusside to some of the solution from the Sodium ignition indicates the presence of Sulphur. The solution may also be tested for sulphide by means of Lead Acetate.

Halogens.

These are identified in the usual way, after removal of Hydrocyanic Acid if necessary by boiling some of the above solution with Nitric Acid.

Phosphorus.

This element can be detected as phosphate after ignition of the substance with Potassium Carbonate and Potassium Nitrate.

It is now possible to decide to which of the following groups the unknown compound belongs:—

- GROUP I. Organic compounds not containing Halogens, Nitrogen, Sulphur or Phosphorus, see below.**
- GROUP II. Compounds containing Halogens** (and free from Phosphorus, Sulphur or Nitrogen), page 200.
- GROUP III. Compounds containing Nitrogen** (and free from Halogens, Sulphur and Phosphorus), page 200.
- GROUP IV. Compounds containing Sulphur** (and free from Halogens, Nitrogen and Phosphorus), page 203.
- GROUP V. Compounds containing Nitrogen and Sulphur** (and free from Halogens and Phosphorus), page 203.
- GROUP VI. Compounds containing Nitrogen and Halogens** (and free from Sulphur and Phosphorus), page 203.
- GROUP VII. Compounds containing Halogens, Nitrogen and Sulphur.** (Phosphorus absent), page 203.
- GROUP VIII. Compounds containing Phosphorus,** page 203.

The distinguishing tests in each group, which should be carried out in the order given, together with a knowledge of the physical properties of the substance should enable it to be identified with the aid of the special tests in the Corroborative Chart. When the groups contain a large number of compounds they are divided, as far as possible, according to their chemical type, which should enable any uncommon medicinal body, not mentioned in the scheme, to be classified.

GROUP I. Organic Compounds not containing Halogens, Nitrogen, Sulphur or Phosphorus.

Tests should be carried out in the order given.

1.—Acids.

By treatment with Sodium Carbonate or by an approximate titration using N/1 Caustic Soda solution and Phenolphthalein it should be determined whether the substance is an acid. A neutral solution of the Sodium Salt is then tested with Ferric Chloride and Calcium Chloride, the behaviour of

some common acids being shown in the following table. The polyhydric phenols, such as Pyrogallic Acid, and also a few acids containing nitrogen, although not belonging to this group, are also included for convenience.

Table of the Common Acids.

REAGENT.	OBSERVATIONS.	ACIDS.
Ferric Chloride.	<i>Purple Colouration.</i> (i.) Not discharged by Acetic Acid.	Salicylic acid. Acetyl-Salicylic acid also gives this on warming with the reagent. Carbolic Acid.
	(ii.) Discharged by Acetic Acid.	
	<i>Red Colouration.</i> (i.) Discharged by HCl to yellow colour.	Formic and Acetic Acids
	(ii.) Not discharged by HCl but by HgCl_2 .	Sulphocyanic Acid.
	(iii.) Not discharged by HCl or HgCl_2 .	Meconic Acid.
	(iv.) Blackened by excess of KOH solution.	Pyrogallic Acid.
	<i>Coloured Precipitate.</i> (i.) Buff coloured. The addition of HCl gives white crystalline body.	Benzoic, Hippuric and Cinnamic Acids.
	(ii.) Reddish-brown ppt. (a) Giving clear solution with HCl. (b) White crystals with HCl.	Succinic and Phthalic Acids. Uric Acid.
	(iii.) Blue - Black giving brown solution with H_2SO_4 .	Gallic and Tannic Acids.
	(iv.) Prussian Blue, discharged by NaOH. (v.) Brown solution giving Prussian Blue on adding SO_2 .	Ferrocyanic Acid. Ferricyanic Acid.
Calcium Chloride to cold solution.	(i.) White precipitate soluble on boiling.	Malonic Acid.
	(ii.) White ppt. soluble in HCl but insoluble in Acetic Acid.	Oxalic Acid.
	(iii.) Crystalline powder soluble in HCl and Acetic Acid.	Tartaric, Fumaric Acids.
Calcium Chloride on boiling.	(i.) White ppt. on adding one drop ammonia solution, and soluble in Acetic Acid.	Citric Acid.
	(ii.) White ppt. on adding equal volume of Alcohol. Soluble in Acetic Acid.	Malic Acid.
	(iii.) Greyish-white ppt. Soluble in HCl to pinkish solution.	Tannic and Gallic Acids.

Other acids which should be tested for are Agaric, Cacodylic, Camphoric, Cholalic, Coumaric. Valerianic, Oleic and Stearic acids have a characteristic odour or appearance.

2. Phenols and Lactones.

The presence of these compounds is indicated by solubility in Caustic Soda solution but not in Sodium Carbonate.

PHENOLS.—Phenol, Thymol, α and β Naphthol, Dima (contains also some nitrogenous matter).

LACTONES, dissolving slowly in hot alkali and reprecipitated by acid:—Coumarin (has characteristic odour and gives yellow solution with Caustic Alkali). Santonin.

3. Aldehydes and Ketones.

Aldehydes reduce ammoniacal silver nitrate and give colour with Schiff's reagent. Ketones and Aldehydes form derivatives with Phenylhydrazine and Semicarbazide, the melting points of which are useful for identification, and many give crystalline compounds with Sodium Bisulphite.

The following should be tested for:—Acetaldehyde, Formaldehyde, Paraform, Benzaldehyde, Acetone, Acetophenone.

4. Esters.

These compounds, when hydrolysed by alkali, yield an acid and an alcohol or phenol.

(i.) Esters derived from alcohols usually have a pleasant odour.

Ethyl Acetate, Amyl Valerianate, Methyl Salicylate, Benzyl Benzoate and Succinate.

(ii.) Esters derived from phenols and used therapeutically are often compounds of either Salicylic Acid or Guaiacol.

Salacetol, Salicyl Salicylate, Betol, Salol, Guaiacol Benzoate, Cinnamate, Carbonate, Camphorate, Salicylate, Valerianate.

5. Hydrocarbons.

These are insoluble in cold Sulphuric Acid, aromatic cpds. have characteristic odour, and must be identified by physical properties.

Benzol, Petrol Ether, Toluol, Xylene, Paraffin.

6. Mercury Compounds.

The substance should be tested for Mercury after destroying organic matter with conc. Sulphuric and Nitric Acids.

Common compounds are the Benzoate, Carbolate, Succinimide, Succinate, Lactate, Oleate, Salicylate; Mercurochrome, Flumerin.

7. Compounds Soluble in Water.—CARBOHYDRATES (except starch and cellulose) *Aliphatic Alcohols*, *Glucosides* (moderately soluble). *Polyhydric Phenols*.

(i.) *Sugars and Glucosides*.

These would have been indicated by Preliminary Test 5. Glucosides likely to be present are:—Aesculin, Digitoxin (not very sol. in water), Salicin, Phloridzin, Strophanthin.

(ii.) *Common Alcohols*.

Methyl, Ethyl, Propyl and Isopropyl, Amylene Hydrate (camphoraceous odour.)

(iii.) *Polyhydric Phenols*.

Resorcin, Pyrogallol.

8. Substances having Characteristic Physical Properties.

The following members of this group can be recognised by properties such as odour and appearance.

LIQUIDS.		SOLIDS.	
SUBSTANCE.	DISTINGUISHING PROPERTY.	SUBSTANCE.	DISTINGUISHING PROPERTY.
Apiol (may however be crystalline)	Green liquid. Peculiar odour.	Aloes, Aloin	Yellowish-brown with characteristic odour.
Amyl Alcohol	Characteristic odour.	Coumarin	Fragrant odour. Sublimes at 100° C.
Capsicin	Reddish-brown oily mass.	Podophyllin	Characteristic odour.
Euresol	Oily substance with slight Acetic Acid odour.	Acetophenone	Odour resembling almonds and jasmine.
Santalol	Characteristic odour.	Eurobin	Brownish pdr. with slight acetic odour.
		Lenirobin	White pdr. with slight acetic odour.
		Terpin Hydrate.	Slightly aromatic odour. Sublimes at 100° C.

Test specially for the neutral compounds Podophyllotoxin, Cantharidin, Elaterin. Also for Anthrarobin.

GROUP II.—Compounds containing Halogens. (Nitrogen Sulphur and Phosphorus being absent).

The following are commonly occurring substances:—

CHLORINE COMPOUNDS.

Ethyl Chloride, Chloroform, Chloral Hydrate, Butyl Chloral, Chloretone, Amylene Chloral, Naphthalene Tetrachlor., Carbon Tetrachlor.

BROMINE COMPOUNDS.

Ethyl Bromide, Bromal Hydrate, Brometone, Bromoform, Camphor Monobromide, Tribromphenol and Bismuth Salt, Phenyl-Sedasprin, Sedasprin.

IODINE COMPOUNDS.

Ethyl Iodide, Thymol Iodide, Iohydrin (oily).

Iodised oils such as Iodinol, Lipiodol.

Aspirodin, Phenyl-Aspirodin.

GROUP III.—Compounds containing Nitrogen (Halogens, Sulphur and Phosphorus being absent).

1. The Alkaloids.

Members of this class of compounds, including some synthetic cocaine substitutes, would be indicated by Preliminary Test 4.

In the following table most of the substances in general use are arranged according to their behaviour with certain reagents, and by testing with these in the order named it is possible to determine rapidly in which group an unknown alkaloid occurs, when it is identified by physical properties and special reactions.

In each test about 2 Cc. of a 1% solution of the alkaloidal salt, or saturated if less soluble, and a few drops of the reagent are used, an immediate precipitate only being noted. Before adding Potassium Ferrocyanide 5%, Platinum Chloride 5%, Potassium Chromate 5%, or Picric Acid, the solution is slightly acidified with dilute Hydrochloric Acid. Perchloric Acid and $\frac{1}{10}$ Potassium Permanganate are added to the neutral solution.

It must be remembered that this scheme is intended only as a guide and results must not be interpreted too rigidly, since uncommon alkaloids are not included, and also anomalous results might possibly occur with impure alkaloids or with any deviation from the above conditions.

REAGENT	ALKALOIDS which give a distinct precipitate with the reagent.	Other Alkaloids which give a distinct ppt., but which would be detected in previous groups.
I. Potassium Ferrocyanide in slightly acid solution.	Apomorphine Emetine Berberine Papaverine Cinchonidine Quinidine Cinchonine Strychnine (Yohimbine if impure).	
II. Perchloric Acid to neutral solution.	(i) Immediately reducing KMnO_4 Aconitine Hydrastine Veratrine (ii) Not reducing KMnO_4 immed. Cocaine Ergotinine Holocain	Berberine. Emetine. Papaverine. Strychnine.
III. Platinic Chloride in slightly acid solution.	Diacetylmorphine Nicotine Quinine	Apomorphine. Berberine. Cinchonidine. Cinchonine. Emetine. Hydrastine. Holocain. Papaverine. Quinidine. Strychnine.
IV. Potassium Chromate in slightly acid solution.	*Yohimbine	All the alkaloids previously mentioned give ppt. except Aconitine, Ergotinine and Nicotine.
V. Pieric Acid in slightly acid solution.	(i) Immed. reducing KMnO_4 Codeine Morphine Ethylmorphine Narcein Gelsemine Eserine (ii) Not immed. reducing KMnO_4 Alypin Hyoscyamine Atropine Benzamine Novocain Homatropine Sparteine Hyoscyne Stovaine	All the alkaloids previously mentioned give a ppt. with this reagent.
VI. Mayer's and Gold Chloride.	Conine Pilocarpine	All the Alkaloids in this table give ppt.

*Yohimbine, if impure, may precipitate in the Potassium Ferrocyanide group.

COLOUR REACTIONS WITH FRÖHDE'S REAGENT.

A few drops of the reagent are added to a little of the dry alkaloid in a white dish, the colour being observed after a few minutes. Colourations, being due to reduction of the reagent, are also given by some non-alkaloidal substances, *e.g.*, Salicin, Phloridzin, Colocynthin.

The following alkaloids give a distinct colour :—

Apomorphine (bluish-green)	Morphine (deep red).
Berberine (dark greenish-brown)	Narceine (reddish-green).
Codeine (bluish-green).	Nicotine (red).
Diacetylmorphine (red).	Papaverine (bluish-green).
Emetine (green).	Quinidine (pale green).
Ethylmorphine (yellow, turning green).	Quinine (pale green).
Hydrastin (green).	Veratrin (red).
	Yohimbine (violet).

The following also behave in some respects like alkaloids :—Pyridine, Quinoline, Phenazone, Piperazine, Piperidine, Phenocoll, Pyramidon.

Microscopically—Ferro- and ferricyanides used to differentiate numerous alkaloids.—W. M. Cumming and D. G. Brown, P.J. ii./25, 141.

2.—Purine Bases.

These are weak bases reacting with only a few alkaloidal reagents, and are characterised by giving the murexide test, see Caffeine, p. 215.

Caffeine, Theophylline, Theobromine and also their compounds with sodium salts such as Theobromine Sodium Salicylate. Uric Acid.

3.—Urea Compounds and Ureides.

Ureides are hydrolised by strong Caustic Potash, slowly in some cases, into the potassium salt of the acid and urea, the latter compound undergoing further decomposition giving Potassium Carbonate and evolving Ammonia. (N.B. Amides, *e.g.*, Acetamide and Chloralamide, also yield Ammonia on heating with alkali solution, but without formation of carbonate.) Note also precipitation with Millon's reagent, *v.* Malourea, p. 227.)

Test for Urea and Urthane (both readily soluble in water) and the ureides Alloxan, Allantoin, Dial, Luminal, Medinal, Proponal, Soneryl, Veronal, etc..

4.—Amines.

Test for primary amines by the carbylamine reaction. Warm the substance with alkali and a little chloroform, and noting any isocyanide odour.

This reaction is not given by primary amines capable of forming non-volatile salts, *e.g.*, Aminophenols, Aminocarboxylic Acids, Aminosulphonic Acids.

If however, after heating, a sample is withdrawn on a glass rod and held in the current of air breathed out from the nose, the carbon dioxide combines with the alkali and liberates the volatile carbylamine derivative, the odour of which soon becomes noticeable.—J.C.S., A. ii./24, 430.

(i) Aliphatic Primary Amines.

After solution of the substance in excess HCl. and treatment with Sodium Nitrite these compounds yield an alcohol on heating, but they are rarely met with except as the amino acids. Asparagine, for example, is converted to Malic Acid by nitrous acid.

(ii) Aromatic Primary Amines.

These bodies form a diazonium compound with Sodium Nitrite and acid, which usually couples with an alkaline solution of β Naphthol forming dyes, and also gives a phenol on heating. Examine for Aniline, Arsamin, Anæsthesine, Phenocoll.

The following give reactions for a primary amine after hydrolysis :—

Acetanilide, Acetyl-p-amido-salol, Phenalgin, Phenacetin.

(iii) Secondary Amines.

Treatment with nitrous acid forms a nitroso compound which can be identified by Liebermann's reaction.

Exalgin gives the secondary amine, methylaniline, after hydrolysis.

The following compounds give colours with nitrous acid :—

Adrenalin	red colour.	Phenazone	green colour.
Methylamino-Oxybenzoate	yellow colour.	Pyramidon	violet colour.

5.—Inorganic Matter Present.

Important compounds are those of Silver, *e.g.* Argyrol, Albargin, Silver Proteinates, Colloidal Silver. The presence of inorganic matter in compounds of this group may denote a metallic cyanide, ferro- or ferricyanide.

Mercury Cyanide and oxycyanide.

6.—Amino-Acids.

These are neutral compounds usually soluble in water and insoluble in alcohol and ether.

Common substances are :—

Acid Hippuric.

Hydrolysed by HCl to Benzoic Acid and Glycocoll.

Asparagine.

Gives Malic Acid on treatment with HNO_2 .

Glycocoll.

Gives deep blue colour with CuSO_4 due to copper glycocoll. FeCl_3 gives intense red colour discharged by acids.

Anthranilic Acid.

Heated with Calcium Oxide yields aniline. Treatment with Nitrous Acid and warming gives salicylic acid.

Betaine.

Usually occurs as the hydrochloride which gives a very acid solution in water.

Fusion with KOH gives Trimethylamine.

Forms a periodide on adding a solution of Iodine.

7.—Esters of Nitrous and Nitric Acids.

Amyl and Ethyl Nitrites have characteristic effect on inhaling. (See Vol. I, p. 165).

Nitroglycerin, Mannitol and Erythrol Nitrates are readily hydrolysed giving a nitrate. Being very explosive they usually occur only in solution or massed with an inert substance.

8.—Nitro-compounds.

Reduction in acid solution gives primary amines which can be identified as described above. Usually poisonous and not used medicinally.

Nitrobenzene (" Oil of Mirbane ") is used as a cheap perfume.

9. Other compounds. Test for Hexamine and compounds, Phenoquin, Cryogenin.**GROUP IV. Compounds containing Sulphur** (Halogens, Nitrogen and Phosphorus being absent).

Sulphocarbates of Zinc and Sodium, Sulphorcinates, Sulphonals, Thiore-sorcin.

GROUP V. Compounds containing Nitrogen and Sulphur (and free from Halogens and Phosphorus).

A solution of the substance should be tested for sulphate and if present the organic base, which is probably alkaloidal, should be examined as described in Group III, p. 200.

Other substances are :—Albumin Tannate, Argyrol, Chinosol, Glycogen, Indigo-Carmine, Proflavine, Saccharin, Bile acids and salts. Thiosinamine, Novarsenobenzol.

GROUP VI. Compounds containing Nitrogen and Halogens (and free from Sulphur and Phosphorus.)

A solution should be tested for ionised halogen, by means of Silver Nitrate, which indicates the presence of a salt of an organic base. The latter if alkaloidal is described in Group III, p. 200.

CHLORINE COMPOUNDS.

Acridine, Arsenobenzol, Betaine Hydrochloride (*v.* above) Chloralamide, Chloramine T, Dichloramine T, Fuchsin, Malachite Green.

Cocaine Substitutes, *e.g.* Alypin, Novocain, Stovaine, etc., are mentioned in Group III, p. 200.

BROMINE COMPOUNDS.

Adalin, Bromethylformine, Bromo-valerianyl-urea, Dibromo-tannin-gelatin.

IODINE COMPOUNDS.

Tetraiodopyrrol.

GROUP VII. Compounds containing Halogens, Nitrogen and Sulphur (Phosphorus absent).

Methylene Blue, Thiosinamine Ethyl Iodide.

GROUP VIII. Compounds containing Phosphorus.

Acid Glycrophosphoric and Salts.

Nuclein, Nucleinic Acid, Lecithin.

CORROBORATIVE TESTS.

The following chart gives the physical constants and characteristic reactions of many medicinal compounds. It will be found useful in confirming results obtained by the preceding method of analysis. The tests with the alkaloidal reagents were carried out in the author's laboratory, and the data obtained are of special interest in dealing with the Purine Bases, which in general do not precipitate, or with non-alkaloidal substances, for example Phenazone, which behave like alkaloids.

Minimum quantities capable of detection.

In revising the table for this edition, attention has been paid to the difficulties in respect of *minute quantities* of the compounds, and in many instances the smallest amount that can be recognised is indicated. These are, of course, the results of our actual trials and investigations.

The Melting Points, Solubilities, etc., are repeated from the body of the book. In other cases solubilities have been determined by customary methods.

In trying the effect of heat about 0.1 Gm. in a 3 by $\frac{1}{2}$ inch test-tube should be used. For the Bromine Water Test, Mayer's Test, Gold Chloride Test, Picric Acid Test and Dragendorff's Test, the 1 in 25 solution of the substance is used, or, if not soluble to that extent, a saturated solution is employed.

For formulæ for preparation of Mayer's, and Dragendorff's Solutions, *vide* pp. 83 and 49.

Gold Chloride Solution is used 1 in 20.

Other Alkaloidal Reagents are the following:—

Ammonium Sulpho-molybdate. — Froehde's Reagent. — Ammonium Molybdate 1 Gm. in Concentrated Sulphuric Acid 100 Cc.

Erdmann's Reagent. — Mix 6 drops of Nitric Acid (Sp. Gr. 1.25) with water 100 Cc., add 10 drops of this to 20 Cc. of Concentrated Sulphuric Acid.

Mandelin's Reagent. — Sulpho-Vanadic Acid. — A 1% solution of Sodium Vanadate in Concentrated Sulphuric Acid.

Mercuric Chloride Solution. — 1 in 20.

Platinic Chloride. — 1 in 20.

Phospho-Tungstic Acid. — Dissolve Sodium Tungstate 100 and Sodium Phosphate 70 in Water 500, and acidify with Nitric Acid.

Phospho-Molybdic Acid. — Sonnenschein's Reagent. — Consists of a solution of Sodium Phosphomolybdate in Nitric Acid, prepared by acidulating a warm solution (50 to 60° C.) of Sodium Phosphate with Nitric Acid, and adding an excess of Ammonium Molybdate Solution. The yellow precipitate is separated, washed with water, acidulated with Nitric Acid and dissolved in a hot solution of Sodium Carbonate (using as little as possible).

The solution is evaporated to dryness and ignited at low red heat till all Ammonium Salts are volatilised, the residue moistened with Nitric Acid and again ignited. The product, consisting of Phosphomolybdate of Sodium, is dissolved in ten times its weight of water.

and Nitric Acid (Sp. Gr. 1.42) added until the precipitate at first produced disappears.

Tannic Acid.—A Solution of Tannic Acid 1 in Water 8, and Alcohol 1, freshly prepared.

Wagner's Reagent.—Iodine in Potassium Iodide. Iodine 5, Potassium Iodide 10, Water 100.

(NOTE.—It is important in testing with this Reagent, *e.g.*, in assaying drugs to determine whether sufficiently extracted, to note that water saturated with Ether and then acidulated gives a precipitate of Iodine on adding this reagent. If a precipitate be obtained in this way confirm by adding water. If it is due to Iodine caused by the Ether it will dissolve again.—*Am. Jl. Ph.*, April '09, 177.)

To save space we have found it best to use FORMULÆ in the chart in place of long chemical names, *e.g.*, HCl, NaOH.

Contractions used in the Chart are as follows:—

a.	=after	mod.	=moderate.
ac.	=acid.	ne.	=neutral.
alc.	=alcoholic	o.	=odour.
alk.	=alkaline.	or.	=orange.
arom.	=aromatic.	pp.	=precipitate.
b.	=before.	pt.	=partially.
bl.	=black.	quick.	=quickly.
bn.	=burns.	react.	=reactions.
br.	=brown.	res.	=residue.
c.	=with.	rediss.	=redissolves.
ch.	=chars.	sat.	=saturated.
col.	=color.	sl.	=slight, slightly.
dec'm.	=decomposes	s.	=sine (without).
dk.	=dark.	sns.	=softens.
dist.	=distillate.	sol.	=solution.
Drag.	=Dragendorff;	str.	=strongly.
eff.	=effervescent.	sub.	=sublime or sublimate
gr.	=green.	v.	=very.
inf.	=inflammable.	vp.	=vapor.
insol.	=insoluble.	vi.	=violet.
m.	=melt(s).	wh.	=white.
misc.	=miscible.	yell.	=yellow.

The ABBREVIATIONS of AUTHORS' NAMES are in general those used in the body of the "Extra Pharmacopœia."

Microchemical identification of some vegetable drugs.—Y.B.P., '24, 274.

NO.	SUBSTANCE.	HEAT.	MPT. °C.	SOL. AQ. (1in-)	SOL. ALC. (1in-)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
1	Acetanilide ...	M. sub. vap. burns.	113	200	4½	Nil.	Nil.	Nil.	Br. pp.
2	Acetone ...	Evap. c. inflam. vap.	—	Misc.	Misc.	Nil.	Nil.	Nil.	Nil.
3	Acetophenone	Evaps., does not ch.	20	V. sl.	Misc.	Nil.	Nil.	Nil.	Br. pp.
4	Acetyl-para- amido-Salol	M. turns yell. and ch. vap.	180 —185	V. sl.	Sl.	Nil.	Nil.	Nil.	Nil.
5	Acid Aceto- Salicyl	M.c. Acetic odor. ch. vap.	135	400	1 in 5	Nil.	Nil.	Nil.	Nil.
6	„ Agaric ...	M. c. eff. ch. br. dist. and inf. vp.	137	Insol.	V. sl.	Nil.	Nil.	Nil.	Nil.
7	„ Benzoic .	M. Sub., Brns. c. irrit. o.	121·5	450	3	Nil.	Nil.	Nil.	—
8	„ Caccodylic	M. ch. Garlic vap. As. flame.	200	½	4	Nil.	Nil.	Nil.	Nil.
9	„ Cam- phoric	M. sub. c. inf. vp.	186	About 200 or more.	About 1½	Nil.	Nil.	Nil.	Nil.
10	„ Carbolic (CRYST.)	M. and evaps. c. inf. vp.	39	12	0·16	Nil.	Bl. pp. comes v. slow.	Nil.	Nil.
11	„ Cholalic (COLALIN)	Part. m. o. o. Ch. c. alk. inf. vp.	Nil.	Sl.	Abt. 1.	Nil.	Nil.	Nil.	V. sl. red- br.
12	„ Cinnamic	M. wh. sub. & inf. vp.	130	Sl.	10½	Nil.	Nil.	Nil.	Nil.

No.	BROM. AQ.	SPECIAL TESTS.
1	Wh. pp.	Hydrolised by HCl or KOH soln. to Aniline and Acetic Acid. 0.1 Gm. boiled with HCl 2 Cc., then mixed with 3 Cc. of Phenol Solution (1 in 20) and 5 Cc. of sat. Chlorinated Lime Sol., turns br.-red changing to blue on adding NH_3 (Indophenol Test U.S.P.). Heated with Boric Acid over a naked flame, gives yell. residue sweet o. Phenacetin gives yell.—Phenazone a pink and o. of Naphthalene. <i>Aniline o. by boiling 3 minutes with 1 Cc. HCl and making Alk. c. NaOH from 0.001 Gm. in 5 Cc. Water.</i>
2	Nil.	Oxidation c. $\text{K}_2\text{Cr}_2\text{O}_7$ & H_2SO_4 gives Acetic and Formic Acids. Combines c. Chloroform in presence of Caustic Alkali to form Acetone-Chloroform: colourless crystals, M.Pt. 96° C. insol. in water. In aq. sol. can be thrown out by salts, e.g., Calcium Chloride. Iodoform Test, v. Urine Examn. <i>0.00025 Gm. in 5 Cc. wtr. satd. c. Am. Chlor. and 1-2 drops 5% Na Nitroprusside and made Alk. c. NH_3—purple in $\frac{1}{2}$ hour.</i>
3	Sl. pp. rediss.	<i>0.01 Gm. in 5 Cc. wtr.</i> With Hydroxylamin HCl forms Acetoxime $\text{C}_6\text{H}_5\text{C}(\text{N.OH}).\text{CH}_3$ (white pp.) M.Pt. 59° C. This by boiling c. Dil. H_2SO_4 in Glacial Acetic Acid is converted into Acetanilide (Beckmann's reaction), and then Aniline (Odor) and Acetic Acid.
4	Nil.	Yields Salicylic Acid on hydrolysis c. NaOH. Is not hydrolised by HCl. Does not give Isonitrile Test, but on adding the Chloroform it gives a br.-red. When hydrolising with dilute NaOH it turns blue, changing to reddish-violet on boiling, the blue reappearing on cooling is changed to red with HCl.
5	No pp.	<i>0.0001 Gm. in 5 Cc. wtr. boiled 2 mins. c. HCl a few drops. Neutralised c. NaOH and one drop Fe_2Cl_6—purple.</i>
6	Nil.	Turns gelatinous and soapy on boiling c. wtr. <i>0.00001 Gm. in 5 Cc. wtr. with 15 Cc. H_2SO_4 cooled and a few drops Syrup added. Purple in a few minutes.</i>
7	Nil.	<i>0.001 Gm. in 0.5 Cc. wtr. light buff pp. c. 1 drop Fe_2Cl_6 T.S. (5%). Further 0.001 Gm. warmed sl. c. 3 drops 25% Formic Acid and the soln. neutralised c. Lime Water and evapd. to dryness. Residue well heated in sm. tube gives odor Benzaldehyde. Lime Water does not pp. an Aq. Soln. either hot or cold. Lead Acet. does not either, but it pps. Benzoates.</i>
8	Nil.	<i>0.005 Gm. in wtr. 5 Cc. c. a few drops Hypophosphorus Acid. Cacodyle odour in a few seconds.</i>
9	Nil.	Gives sublimate of anhydride, M.Pt. 217° , on heating.
10	Wh. pp. rediss. at first.	To 0.001 Gm. in 10 Cc. of water add 1 drop of 10% Sod. Nitrite sol. and pour on to H_2SO_4 . A coloured zone—red above, green below—appears at the junction. Bleaching Powder to aqueous solution gives violet.
11	V. sl. pp.	Gives blue unstable compounds with Iodine resembling Starch Iodide.—Watts, <i>q.v.</i> for further information. <i>0.0001 Gm. in 5 Cc. Water responds as Ac. Agaric. c. H_2SO_4 and Syrup.</i>
12	Nil.	<i>0.0025 Gm. oxidised c. $\text{K}_2\text{Mn}_2\text{O}_8$ to Benzaldehyde. Can be reduced by Sodium Amalgam to Hydrocinnamic Acid (β.phenyl-propionic Acid). Detected in presence of Benzoic Acid by suspending in 5% Uranium Acetate solution and exposing to sunlight,—in a few mins. odour of Benzaldehyde is evolved, and brown ppt. forms.—Allen.</i>

No.	SUBSTANCE.	H. T.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
13	Acid Citric ...	M. clear ch. inf. vp.	135 -154	0.6	1½	Minute crystals a. a while.	Nil.	Nil.	Nil.
14	„ Coumaric	M. ch. c. inf. vp.	200	600	12 (or less).	Nil.	Nil.	Nil.	Nil.
15	„ Cresylic	Evaps., vp. burns	—	70	Misc.	Nil.	Bl. pp. comes slow.	Nil.	v. sl. pp.
16	„ Gallic ...	Part m. & ch. Or. sub. & br. vp. bns.	Nil.	100 (ap prox.)	5	Nil.	Dirty br. pp.	Nil.	Nil.
17	„ Glycero- phosph.	Evaps. Res. effs. & ch. vp. bns.	—	Misc.	Misc.	Nil.	Nil.	Nil.	Nil.
18	„ Hippuric	M. to clear, liq. ch. c. inf. & alk. vp.	187	v. sl.	30	Nil.	Nil.	Nil.	Nil.
19	„ Malic ...	M.c. sub.	Abt. 180	1	1½	Nil.	Nil.	Nil.	Nil.
20	„ Meconic	Ch. c. wh. sub. & vp.	Nil.	Sl.	48	Nil.	Nil.	Nil.	Nil.
21	„ Nucleinic	Ch. c. o. of burnt feathers.	Nil.	Al- most insol.	Insol.	Nil.	Nil.	Nil.	Nil.
22	„ Oleic ...	Distils c. sl. residue ch.	—	Insol.	55	Nil.	Nil.	Nil.	Nil.
23	„ Oxalic ...	M. & sub.	102	9	8	Nil.	Nil.	Nil.	Sl. pp.
24	„ Pyrogallie	Sub. c. decomp.	132	2	1	Nil.	Re- duces	Nil.	Nil.
25	„ Salicylic	Sub. vp. bns.	156	500	3	Nil.	Nil.	Nil.	Nil.
26	„ Sclerotic	Ch. alk. vp. bns.	Nil.	Prac. all	Insol.	Nil.	Sl. br. pp.	Nil.	Red br. pp.
27	„ Stearic ..	Sub. vp. bns.	50—55	Insol	18	Nil.	Nil.	Nil.	Nil.
28	„ Succinic	M. & vol.	182	20	9	Nil.	Nil.	Nil.	Br. pp.

NO.	BROM. AQ.	SPECIAL TESTS.
13	Nil.	Denige's Test. Add a solution of Mercuric Sulphate (HgO dissolved in H_2SO_4) and H_2SO_4 to the citrate sol. On warming, this solution decolorises KMnO_4 , giving white pp. <i>Visible with 0.0001 Gm. in 5 Cc. wtr.</i> Tartaric Acid gives none. A solution is boiled with a little $\text{K}_2\text{Cr}_2\text{O}_7$, and, after cooling, Acetic Acid and Na Nitroprusside added and then NH_3 to form a layer. Acetone from the Citric Acid gives a violet-red col. at the surface of contact.—J.C.S., A. ii./25,246.
14	Yell. pp.	Melted with KOH gives Salicylate and Acetate, Aqueous solutions of Alkaline Coumarates are fluorescent.
15	Wh. pp.	0.0001 Gm. in 5 Cc. wtr. turns brownish with $\text{NaNO}_2 + \text{HCl}$, changing to reddish-brown on adding a few drops NaOH soln.
16	Nil.	0.000125 Gm. in 5 Cc. wtr. on adding Lime Water gives pink; 0.00025 Gm. gives purple; 0.0005 Gm. gives blue grey pp. 0.005 Gm. in 5 Cc. wtr. turns brown with NaNO_2 alone.
17	Nil.	0.001 Gm. in 5 Cc. wtr. boiled 3 mins. c. HCl gives Phosphoric Acid and Glycerin. Usually occurs as a 20% aqueous solution.
18	Nil.	<i>Boil 0.01 Gm. a few minutes with Caustic Soda 1 Cc. and neutralise c. HCl. Half this soln. gives buff pp. c. Fe_2Cl_6 (Benzoate). Acidify the other. Evap. to dryness, extract the Glycocol. c. Acetic Ether. This dissolves freshly pptd. Copper Carbonate c. deep blue color. Copper Benzoate if present does not interfere and if nec. Benzoic Acid can be removed with Ether in which Glycocol is insol.</i>
19	Nil.	Treated with Potash and Bromine, Bromoform is formed.
20	Decols. first few drops of test.	An aqueous solution with Ferric Chloride gives a red colour not discharged by Hydrochloric Acid or Mercuric Chloride (distinction from Thiocyanate).
21	Nil.	Schmidt gives some information on the various Nucleinic Acids (animal, plant, yeast, etc.), but no very distinct analytical reactions. Nucleinic Acids boiled with H_2SO_4 dilute c. decomp. products yield Phosphoric Acid, Carbohydrates and Xanthin bases (Xanthin, Guanin, etc.). (Our tests were conducted with slightly brown Nucleinic Acid.)
22	Nil.	Characteristic odour. Solidifies at $+4^\circ\text{C}$. Pure Oleic Acid, as such, does not redden Litmus, but does in Alc. sol. Nitrous Acid converts it into the stereo-isomeric Elaidic Acid in crystalline leaflets. M.Pt. 45°C .
23	Nil.	A neutral Salt soln. gives pp. with sol. lime salt, insol. in Acetic Acid, but sol. in HCl . $\text{K}_2\text{Mn}_2\text{O}_8$ is decolorised in hot soln.
24	Nil.	In presence of Caustic Alkali rapidly darkens. (Takes up Oxygen.)
25	Wh. pp.	<i>Violet produced by 0.0000025 Gm. in 1 Cc. wtr. c. 1 drop Fe_2Cl_6 (5%) is just visible; 0.000005 Gm. is distinct. Use narrow tube on white ground. Green Cu. Salicyl by adding CuSO_4 to soln. not distinct for small qties. 0.00005 Gm. c. 0.5 Gm. $\text{Ca}(\text{OH})_2$ htd. red in sm. tube; Phenol odor.</i>
26	Br. pp.	Precipitated by Tannic Acid and Phosphomolybdic Acid.—Schmidt.
27	Nil.	Acid number 200—210.
28	Nil.	Forms fluorescein dyes when heated with Resorcin and Sulphuric Acid.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
29	Acid Tannic	Part m.ch. orange sub. & br. inf. vap.	Nil.	1½ slowly	1	Nil.	Grnsh bl. pp.	Nil.	Nil.
30	„ Tartaric...	M. ch. vp. bns.	162— 165	0·8	2½	Cystls aft. a. while.	Nil.	Nil.	Nil.
31	„ Valerianic	Evap. c. str. o. vp. bns.	—	30	All props.	Nil.	Nil.	Nil.	Nil.
32	Aconitina ...	Ch. c. acrid vp.	190 apprx.	v. sl.	40	Wh. pp.	Yell. pp.	Yell. pp.	Br. pp.
33	Acriflavine ...	Bl. Red ac. vap.	—	5	40	Buff. pp.	Red sol. fluor.	Buff. pp.	Br. pp.
34	Adalin ...	Part sub ac. vap.	116	Sl. sol. cold more sol. hot.	20	Nil.	Cryst. pp. (No pp. c. 1 in. 1,000)	Cryst. pp. (Not c. 1 in. 1,000)	pp. (Not c. 1 in 1,000)
35	Adrenalin ...	Red'sh ch. alk. vap.	—	v. sl.	v. sl.	Nil.	v. col.	Nil.	Nil.
36	Æsculin ...	M. c. sl. eff. ch. yel. dist. vp. bns.	—	sl.	sl.	Nil.	blue col.	Nil.	Nil.
37	Æthyl Bromid ...	Evap.	—	85	Misc.	Nil.	Nil.	Nil.	Nil.
38	Æthyl Chlorid ...	Evap.	—	Sl.	Read- ily.	Nil.	Nil.	Nil.	Nil.
39	Æthyl Iodid .	Evap.	—	400	Misc.	Nil.	Nil.	Nil.	Nil.
40	Abumin Tannas ...	Ch. c. o. of burnt feathers Br. alk. vp. brns.	—	Sl.	Sl.	Nil.	Dark dirty br. pp.	Nil.	Nil.
41	Alcohol Methylic	Evap.	—	Misc.	Misc.	Nil.	Nil.	Nil.	Nil.
42	Aldehyde Abs	Evaps.	—	Misc.	Misc.	Nil.	Nil.	Nil.	Nil.
43	Allantoin ...	M. ch. alk. vap.	De- comp.	260	5000	Nil.	Nil.	Nil.	Nil.
44	Alloxan ...	M. to dark red br. liq. ch. & HCN. o.	—	Sl.	Sl.	Nil.	Sl. blue col.	Nil.	Nil.

No.	BROM. AQ.	SPECIAL TESTS.
29	V. s'ly stringy pp.	Gives pp. c. Gelatin, $\text{Pb}(\text{NO}_3)_2$ (c. 0.0001 Gm.), $\text{Bi}(\text{NO}_3)_3$, (ditto), and Ammoniacal Copper solution.—(Distinctions from Gallic Acid). 0.0001 Gm. gives bl. c. Fe_2Cl_6 . Is hydrolised into Gallic Acid by boiling with dilute Sulphuric Acid. Gives brown with NaNO_2 .
30	Nil.	To a neutral soln. add AgNO_3 , when white Silver Tartrate is pptd. On just dissolving in dilute NH_4OH and warming, a silver mirror is obtained if test-tube is clean.
31	Nil.	This acid has a characteristic, unpleasant odour. Fused CaCl_2 separates the acid from its aqueous solution.
32	Yell. pp.	1 mgm. warmed with 4 drops of H_2SO_4 , S.G. 1.75, and a crystal of Resorcin added, the liquid becomes reddish-violet in about 20 mins. 0.000001 Gm. produces tingling and numbing on the tongue. 0.0001 Gm. c. Acetic Acid red pp. c. $\text{K}_2\text{Mn}_2\text{O}_8$.
33	Nil.	Dilute solution is yellow, strong solutions red with deep green fluorescence; gives HCl on heating with H_2SO_4 , as distinct from Proflavine.
34	Nil.	H_2SO_4 gives HBr on warming (Br c. H_2SO_4 and MnO_2). Heating with NaOH and acidifying c. H_2SO_4 , Acetic Acid odour. CO_2 is evolved. Does not pp. with Millon's Reagent after acidifying.—See Malourea. Sat. aq. soln. gives yellow colour and then an orange pp. with Nessler's Reagent. Dial, Malourea, Medinal and Propional do not react except after fusing with KOH . Bromural and Luminal solns. give slight colour, but effect with Adalin is distinctive.
35	Nil.	<i>Several of these tests visible c. 0.0005 Gm.</i> NaNO_2 alone gives red colour. For Phosphoretted Hydrogen odour with NaOH ,— <i>vide</i> Organotherapy. Reduces AgNO_3 solution.
36	Dp. rd. col. to prplsh. opalescence.	Yields Glucose and Æsculetin on hydrolysis and then reduces Fehling's. Gives blood red col. when treated with HNO_3 and then excess of NH_4OH . Gives blue fluorescence in alk. sol. Treated with H_2SO_4 and then sol. of NaOCl gives violet col.—Allen, Watts.
37	Nil.	Differs from the poisonous Ethylene Bromide by Sp. Gr. and boiling point.— <i>Vide</i> Vol. I., p. 836.
38	Nil.	This is a gas at ordinary temperatures and pressures, boiling point 12.5°C .
39	Nil.	Iodine liberated on shaking with water containing a little fuming Nitric Acid. Boiling point $71-72^\circ \text{C}$.
40	Nil.	Nitrogen content 8%.— <i>Vide</i> Vol. I., p. 95, for estimating its capabilities of withstanding Pepsin and Hydrochloric Acid.
41	Nil.	Oxid. c. Chromic Acid yields Formic Acid. Method of detection in Ethyl Alcohol, see Ethyl alcohol this vol.
42	Nil.	Shaken c. conc. Sodium Bisulphite soln. gives cryst. addition-product $\text{CH}_3\text{CH.OH.SO}_3\text{Na}$ decompd. by acid or alkali. Combines c. Phenyl-hydrazin forming Ethylidenphenylhydrazone. Combines c. NH_3 forming additive compd.
43	Nil.	Conc. Furfural soln. to which a little HCl added gives violet c. Allantoin aq. soln. Mercuric Nitrate (not Chloride) a pp. as c. Urea.
44	Nil.	Aqueous soln. slowly turns red when applied to the skin. Solid NaOH turns alc. soln. blue, which is decolorised by wtr.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
45	Aloes Curaçao	Part m. br. yell. vp. bns. br. dist.	—	Part. sol.	6 in- com- plete.	Nil.	Red col.	Nil.	Br. pp.
46	„ Cape ...	Part m. br. vp.bns.	—	Part, sol.	2	Nil.	Br. pp.	Nil.	Br. pp.
47	„ Soc. ...	Part. m. br. yell. vp. bns. br. dist.	—	Part, sol.	8 in- com- plete.	Nil.	Nil.	Nil.	Br. pp.
48	Aloin ...	M. & ch. vp. bns.	145	140	20	Nil.	Red col.	Nil.	pp.
49	Alypin ...	M.c. eff. then ch. Alk.vp. bns	169	1	4	Wh. pp.	Buff. pp.	Yell. pp.	Red- br. pp.
50	Amylene Chloral Sol. 1 : 1	Evaps. vp. bns.	—	Misc. c. l. thr'wn out againc 2,r'dis. in 3	Misc.	Nil.	Nil.	Nil.	Nil.
51	Amylene Hydrate	Evaps.	—	8	Misc.	Nil.	Nil.	Nil.	Nil.
52	Amyl Nitris...	Evaps. sl. res. ch.	—	Sl.	Misc.	Br. col.	Nil.	Nil.	Bl. pp.
53	Amyl Val- erianas	Evaps. vp. bns.	—	v. sl.	Misc.	Nil.	Nil.	Nil.	Nil.
54	Anæsthesine	M. evap. vp. bns.	89	Sl.	8	Nil.	Br. pp.	Nil.	Nil.
55	Aniline ...	Evaps.	—	30	Misc.	Nil.	Dark br. pp.	Nil.	Br. pp. to dirty yell.
56	Anthrarobin	Br. sub. wh. res.	—	v. sl.	80	Nil.	P'rple col.	Nil.	Nil.
57	Antim. Pot. Tart.	Blackens, grey-wh. sub.	—	17	insol.	Nil.	Nil.	Nil.	De- color- ises.
58	Antipyrin, see PHENAZON	—	—	—	—	—	—	—	—
59	Apiol (Green Liquid)	Goes br. br. dist.	—	Prac. insol.	Part.	Nil.	Nil.	Nil.	Br. pp.

NO.	BROM. AQ.	SPECIAL TESTS.
45	Yell. pp.	Curaçao Aloes may be distinguished by the Cupraloin reaction, not given by other varieties. To 10 Cc. of 1 in 1,000 aq. soln. add 1 Cc. 5% CuSO_4 and 1 Cc. sat. NaCl soln. and a few drops of Prussic Acid—a deep claret col. is produced.
46	Yell. pp.	Ammonia changes an Alc. soln. of Barbaloin and Socaloin br. red and Nataloin carmine red.
47	Yell.	Reactions given by all Aloes. Treat 0.5 Gm. with 100 Cc. hot water, cool and filter. Heat 20 Cc. of filtrate on w.b. c. small pieces of Sod. Peroxide. Brown turning cherry red produced which may be shaken out c. Ether.
		Aloes distinguished from Rhubarb, Cascara, etc., by not being pptd. with basic Lead Acetate.
		Aq. sols. of Aloes give a green fluorescence c. Borax.
48	Yell. pp.	Dissolves in NH_3 and caustic alks., the yellow soln. rapidly turning red c. green fluorescence. Ferric Chloride to Alc. soln. brown-green colour.
		<i>One drop of CuSO_4 sol. added to 0.00005 Gm. in 5 Cc. Aq. gives yell. col. changed to red by 0.5 Cc. of satd. NaCl and to violet by 1 Cc. 90% Alc.</i>
49	Yell. pp.	Behaves similarly to Cocaine, <i>q.v.</i> this vol. Can be distinguished by fact that 4% solution does not precipitate with Platinic Chloride in presence of HCl .
50	Nil.	This is an oily liquid formed by adding Chloral to Amylene Hydrate.
51	Nil.	This compound has a pungent taste, and odour resembling Camphor. Boiling point $99-103^\circ$. It solidifies to crystals on cooling to a low temperature.
52	Nil.	Characteristic odour,—produces flushing of face on inhalation, for further information, <i>v. Vol. I., p. 152 et seq.</i> , and this Vol. <i>antea</i> .
53	Nil.	Yields Amyl Alcohol and Valeric Acid on hydrolysis.
54	Yell. pp.	Hydrolysis gives Ethyl Alcohol and p-amino-benzoic Acid. Gives isonitrile reaction, <i>cf.</i> Acetanilide.
55	Wh. pp.	To neut. or sl. alk. aq. sol. add Sodium Hypochlorite or Chlorinated Line sol.—purple violet, even in 1 in 26,000—changing to dirty red. Avoid excess of Reagent (Runge). When this change has occurred, add Ammoniacal Phenol sol., return of blue col. (Jacquemin-Dragendorff) even in 1 in 66,000. Aq. Chromic Acid sol. according to concentration gives green, blue or almost black (Fritzsche).
56	Dirty br. pp.	Easily soluble in Caustic Alkalis and Ammonia, giving yellowish solution gradually changing to green or blue owing to formation of Alizarin.
57	Nil.	0.00005 Gm. in 5 Cc. <i>utr. made acid gives orange color with H_2S. More gives pp. soluble in Ammonium Sulphide and KOH. On "Marshing," black mirror insol. in Na Hypochlor. soln. With Lime Water white pp. soluble, when freshly precipitated, in Acetic Acid and Ammonium Chloride.</i>
58	—	—
59	Nil.	Apiol occurs as a green liquid with peculiar odour and taste and also as white crystals, M.Pt. 30° , with parsley-like odour. Sol. in H_2SO_4 c. bl. red col.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIO- RIC.	DRAG.
60	Apocodeine HCl.	Smell of burnt feathers.	Part. a 90 De- comp. over 200	1	1	Dirty buff. pp.	Dirty br. pp.	Yell. pp.	Br. pp.
61	Apomorphine HCl.	Ch. c. wh. vap.	—	60	51	Wh. pp.	Br.rd. pp.	Yell. pp.	Br.pp.
62	Arbutin ...	M. c. sl. eff. then ch. br. dist. & vp. bns.	166	10	13	Nil.	Gr.col. c'm'ng slowly to br. pp.	Nil.	Nil.
63	Argenti Lactas	ch.vp.bns.	Nil.	18	500	Yell. pp.	Light br. pp.	Sl. pp.	Br.pp. to wh.
64	Argenti Proteinas	Ch. br. dist. alk. vp. bns.	—	Imper- fectly.	V. sl.	Light- ens in col.	Nil.	Yell. flocc. pp.	Br.pp. turn- ing wh.
65	Argyrol ...	Swells up & Ch.	Nil.	All prop.	Insol.	Nil.	Bl. pp.	Br. pp.	Br. pp. to or.
66	Arrhenal ...	Ch., bl. sub. garlic o.	Nil.	1	350	Nil.	Nil.	Nil.	Nil.
67	Arsamin ...	Ch. bl. sub. & alk. vp.	—	6	125	Nil.	Br. col.	Nil.	Br. pp.
68	Arsenobenzol	Ch. ac.vp. and odor.	—	Read- ily.	sl.	Yell. pp.	Or'nge	Yell. pp.	Nil.
69	Asparagin ...	Red. br., alk. vp.	—	50	Insol.	Nil.	Nil.	Nil.	Nil.
	Aspirin <i>see</i> Ac. Aceto- Salicyl.	—	—	—	—	—	—	—	—
70	Aspriodine ...	M., ch. o. Iodo- Phenol	154	v. slight	16½	Nil.	Nil.	Nil.	Nil.
71	Atropine Methyl Brom.	M. c. sl. eff. ch. br. dist. irrit. vap.	214	1	8	Wh. pp.	Red. yell. pp.	Red. yell. pp.	Red. br. pp.
72	Atropine and Salts	Base m. and sub. b. ch. salts m. and ch.	Base 115 Sulph. 187	Base 300, Sulph. ½	Base 3, Sulph. 3	Wh. pp.	Buff. pp.	Yell. pp.	Red br. pp.

No.	BROM. AQ.	SPECIAL TESTS.
60	Dirty br. pp.	Occurs usually as a yellowish or greenish-grey hygroscopic powder. Apocodeine gives a characteristic blood-red colour with Nitric Acid.
61	Re pp.	On adding Ammon. Persulph. and Sod. Bic. to aq. soln. and shaking c. CHCl_3 the latter becomes a red or violet. Detects 1 in 100,000. J.C.S., A. ii./24,798. Sol. in NaOH rapidly becomes red and gradually bl. Acquires a gr. tint exposed to light and air and dissolves in Nitric Acid c. purple colour.
62	Yell. pp. c. excess br.	Hydrolysed by dilute Sulphuric Acid into Glucose and Hydroquinone. Diazo Test—yellow with HCl and NaNO_2 turning red with Sodium Hydrate.
63	Wh. pp.	Residue gives reaction for Silver.
64	Wh. pp.	Ammonium Sulphide turns sol. blackish brown without pp. To 2 Cc. of soln. (1 in 20) add 1 drop of 30% Acetic Acid, white pp., soluble in excess. Residue on incineration gives reactions for Silver. (Contains about 8%). Picric Acid precipitates. 10 Cc. of 1% aq. soln. c. 5 Cc. NaOH soln., becomes violet in a few minutes on adding 2 Cc. 2% CuSO_4 soln.
65	Col. blchd. wh. pp.	Contains about 30% Silver, which can be detected in the residue. Estimate by means of Ammonium Thiocyanate, after destroying organic matter with H_2SO_4 and HNO_3 .
66	Nil.	0.0005 Gm. in 5 Cc. wtr. gives a white pp. with Silver Nitrate, a violet pp. with Cobalt Nitrate and a white pp. on warming with Calcium Chloride (distinction from Sodium Cacodylate).
67	Wh. pp.	0.001 Gm. in 5 Cc. wtr. reduces $\text{K}_2\text{Mn}_2\text{O}_8$ and Gold Chloride. Ferrous Sulphate gives an olive-green pp., and Sodium Hypobromite a bluish-red col. Diazo test gives positive reaction.
68	Nil.	The Arsenic content can be estimated by the methods given under Arsenium, <i>q.v.</i> for further data. The yellow powder is very unstable in air.
69	Nil.	In alk. soln. is lævorotatory; in acid, dextro. Copper Hydrate is dissolved on boiling, forming blue soln., depositing on cooling Asparagin-Copper $(\text{C}_4\text{H}_7\text{N}_2\text{O}_2)_2\text{Cu}$. Insoluble in Ether.
70	Nil.	Heat c. H_2SO_4 gives off Iodine. Heat c. NaOH, acidify and add FeCl_3 —violet colour.
71	Yell. pp.	Gives Vitali's Reaction, <i>vide</i> Atropine, and Bromide reactions with Silver Nitrate.
72	Orange pp.	1 Mgr. warmed with 2 Cc. HgCl_2 in 50% Alc. causes deposition of HgO (c. some Hg_2O)—Gerrard. Dilates the pupil even 1 in 130,000. Responds to Vitali's Reaction .—Evapor. a trace of Atropine (or a salt) in a porcelain dish with a few drops of fuming HNO_3 a yell. residue is produced which on moistening with Alc. KOH (1 in 10) produces a violet col. Strychnine does the same on applying 4% Potash, but the col. is evanescent. Veratrin gives red vi. or or. red. Atropine Sulphate .—Gives Atropine Gold Chloride. M.Pt. 136—138° C. 0.01 mgr. found by Vitali.—Jl. Ph Exp:Th., Nov., '25, 267.

NO.	SUBSTANCE.	HEAT.	M.PT. °C	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
73	Barbitone <i>see</i> Malourea	—	—	—	—	—	—	—	—
74	Benzol ...	Evap. vp. bns.	Nil.	Insol.	0.33	Nil.	Nil.	Nil.	Nil.
75	Benzyl Benzoate	Distils un- changed.	20	Insol.	Misc. ible.	Nil.	Nil.	Nil.	Nil.
76	Betaine HCl.	Part m., ch. c. eff. and alk. vp. bns.	—	2	About 20	Nil.	Nil.	Cryst. pp. in conc. Nil in dil- lute	Br. pp.
77	Betol. ...	M. turns yell. pt. evap. ch. vp. bns.	95	Alm'st insol.	Sl.	Nil.	Nil.	Nil.	Nil.
78	Bismuthi Benzoas	Bl. c. yell. sub. and wh. vp. c. Benzoic o.	Nil.	Al- most insol.	Al: most insol.	Nil.	Nil.	Nil.	Nil.
79	„ Citras ...	Bl. c. bl. sub.	Nil.	Alm'st insol.	Insol.	Nil.	Nil.	Nil.	Nil.
80	„ Oxy-Iodo- gall.	Iodine vapour bl.	Nil.	v. sl. Iodide & Gallic Acid go into sol.	In- com- plete- ly sol.	Nil.	Yell. pp.	Nil.	Nil.
81	„ Salicyl....	Blackens, vp c. o. of Phenol bns.	Nil.	Alm'st insol.	Alm'st insol.	Nil.	Nil.	Nil.	Nil.
82	„ Subgallas	Goes bl. vp. bns.	Nil.	Insol.	Insol.	Nil.	Nil.	Nil.	Nil.
83	Bromal- hydrate	M. wh. vp. cols. flame green	54	2½	½	Nil.	Nil.	Nil.	Nil.
84	Bromethyl Formine	Eff. ch. c. alk. vp.	200 (Schmidt)	0.6	25	Yell. pp. chang- ing to wh.	Br. yell. pp.	Cryst. pp. come slowly.	Red br. pp.
85	Brometone ...	M. sub. & ch. c. v. irritating vap.	167	200	1	Nil.	Nil.	Nil.	Nil.
86	Bromoform .	Dist. then ch. c. br. vp. Brom odor.	—	Sl.	Misc.	Nil.	Nil.	Nil.	Nil.

No.	BROM. AQ.	SPECIAL TESTS.
73	—	—
74	Nil.	To distinguish from Petroleum Benzin notes solubility in Alc. Benzol is sol. c. half vol. of Alc. 90%, but Petrol Benzin requires 5 to 6 vols. (using 'Petrol' more). 1 Cc. Petrol Benzin added to 5 to 10 Cc. of a mixture of 2 parts HNO_3 and 1 part H_2SO_4 —warm slightly:—Benzol gives red vp., yell. nitro compds., then dilute c. 10 to 15 vols. wtr, o. of Bitter Almonds, esp. on well diluting. Petrol. Benzin by this is hardly affected. For Dragon's Blood Test, <i>vide</i> Vol. I., p. 309.
75	Nil.	Decomposes into Benzyl Alcohol and Sodium Benzoate on boiling with NaOH. Benzyl Succinate melts at 45° C.
76	Pp. rediss. at first.	Gold salt melts at 224° C. This salt has a strong acid reaction and taste. Fusion with KOH gives Trimethylamine.
77	Nil.	Alcoholic solution gives violet colour with Ferric Chloride. Hydrolysis gives β -Naphthol and Salicylic Acid.
78	Nil.	Identify Bismuth in the residue and separate Benzoic Acid by heating salt with alkali, filtering and acidifying.
79	Nil.	Sol. in NH_3 and Alkali Citrates. Dissolved in Aq. NH_3 and evaptd., Bismuth Ammonium Cit. is formed. Gives Bismuth and Citrate reactions.
80	Nil.	Easily soluble in Mineral Acids and Caustic Alkalis. Gradually turns red in moist atmosphere. Concentrated H_2SO_4 liberates Iodine vapour.
81	Yell. pp.	Identify Bismuth and Salicylic Acid. For estimation of Salicylic Acid, <i>v.</i> this Vol. <i>antea</i> .
82	Nil.	NaOH dissolves with yellow colour—turning red. Identify Gallic Acid by means of Ferric Chloride after removal of Bismuth, such as by H_2S .
83	Nil.	Decomposes at 100–110°C. into Bromal and water.
84	Yell. pp.	Heated with Caustic Soda solution gives odour of Formalin.
85	Nil.	Reacts like Chloretone, <i>q.v.</i>
86	Nil.	Has odour resembling Chloroform, from which it is easily distinguished by Sp. Gr. and B.Pt.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
87	Bromo- Valerianyl- Urea.	M. ch., orange sub. and vp. bns.	145	Sl.	10	Nil.	Nil.	Nil.	Nil.
88	Butyl Chloral	Sub. totally.	78	43	2	Nil.	Nil.	Nil.	Nil.
89	Caffeine ...	Sub. & m.	236	80	40	Nil.	Sl. pp.	Nil.	Br.. pp.
90	Caffeine Citras	M. ch. c. br. dist. & sl. vp. bns. c. Phenol o.	Abt. 160	33	25	Nil.	Sl. pp.	Nil.	Br. pp.
91	Caffeine Sodio- Salicyl.	Part M. sub c. alk. vap.	Nil.	2	40	Nil.	Nil.	Nil.	Br pp.
92	Calcii di- Bromo- behenas	Part m. ch. c. gr. br. dist. vp. bns.	Abt. 230	Insol.	Pract. insol.	Nil.	Nil.	Nil.	Nil.
93	Calcii Gly- ceroph.	Ch. acrid vp. bns.	Nil.	About 1 in 22	Al- most insol.	Nil.	Nil.	Nil.	Nil.
94	Calcii Lactas.	M. swells & ch.	Nil.	15 or less when fresh.	Insol.	Nil.	Nil.	Nil.	Nil.
95	Calcii Sac- charas	Ch. c. caramel o.	Nil.	10	Insol.	Nil.	Sl. yell. pp.	Nil.	Sl. br. pp.
96	Camph. Monobrom.	M. c. camph. o. & sub.	76	Insol.	18	Nil.	Nil.	Nil.	Nil.
97	Cantharidin...	M. sub. vp. bns.	218	400	Sl.	Nil.	Nil.	Nil.	Nil.
98	Capsicin ...	Boils, irrit. vp. bns.	—	V. sl.	Misc.	Nil.	Nil.	Nil.	Red br.
99	Carbamide, See UREA	—	—	—	—	—	—	—	—
100	Chinolin ...	Evaps. & vp. bns.	—	Sl.	Misc.	Wh. pp.	Crm. pp.	Yell. pp.	Red- br. to bl.
101	Chinazol ...	M. c. eff.	172	1	Sl.	Crm. pp.	Buff. pp.	Yell.	Red- br. to bl.
102	Choralamid	M. sub. c. chloral o.	115	20	2	Nil.	Nil.	Nil.	Nil.

No.	BROM. AQ.	SPECIAL TESTS.
87	Nil.	Odour like Bromal on heating. Dissolves in Caustic Alkali soln. and is pptd. by acids. After heating c. NaOH and acidifying residue c. H_2SO_4 , CO_2 liberated c. Valerianic odour. Millon's gives pp. (cf. Malourea). Nessler's Reagent c. Satd. Solution gives only slight colour and pp. (cf. Adalin), but after fusing c. KOH and dissolving in Aq. there is the usual effect.—W.H.M., 1920.
88	Nil.	Nitric Acid converts it into Trichlorbutyric Acid, M.Pt. $44^\circ C$.
89	Nil.	<i>On evaporating 0.0001 Gm. to dryness with Chlorine Water a reddish-brown spot is obtained, which turns violet-red with Ammonia (Murexide Test). Heated with HNO_3 forms Cholestrophan.</i>
90	Nil.	The aqueous solution is acid owing to hydrolysis. All the Citric Acid present can be titrated with Caustic Soda using Phenolphthalein as indicator. Murexide test as above.
91	Wh. pp.	Caffeine can be estimated by extraction with boiling Chloroform. 0.0001 Gm. gives Murexide and Fe_2Cl_6 reaction. Gives reactions of Caffeine and Sodium Salicylate, q.v.
92	Nil.	No distinctive test—general properties must be taken into consideration.
93	Nil.	Identify Calcium and Phosphate after hydrolysis with acid.
94	Nil.	Acidify a 1 in 20 solution with Sulphuric Acid, add Potassium Permanganate and heat—the odour of Acetaldehyde should be developed.—U.S.P.
95	Nil.	To a suspension of a small quantity in 10 Cc. of water add 5 Cc. HCl and 0.1 Gm. Resorcin in 5 Cc. After shaking, place in boiling Aq. 5 minutes—pink to deep red colour. When used in cream it can be detected thus, using 10 Cc.
96	Nil.	Alc. KOH has no action, but Silver Oxide in presence of $CHCl_3$ decomposes it. Heated with 4 times its quantity of HNO_3 on sand-bath forms Camphoric Acid and Brom-Nitro-Camphor.—Rhombic prisms almost insol. in Alcohol.—M.Pt. $105^\circ C$.
97	Nil.	Boiled with Soda and Potash forms Cantharidates. An exceedingly minute quantity of Cantharidin will produce a blister.
98	Nil.	Identified by general properties (see Vol. I., p. 272).
99	—	—
100	Yell. pp.	Quinoline, B.Pt. $236-238^\circ C$. A mixture of H_2SO_4 and fuming HNO_3 produces crystallised Nitro-Chinoline $C_9H_6.N.NO_2$. On w. b. H_2SO_4 produces mainly Cryst. o-Chinoline-Sulphonic Acid— $C_9H_6.N.SO_3H$. The amorphous pp. c. Mayer can be converted into yell. needles on adding HCl.—Characteristic.—Allen.
101	Yell.	Diazo Test gives slight brownish-red. See also Vol. I., pp. 316, 317.
102	Nil.	Water slightly warm decomposes. Caustic Alkalis decompose it into Chloroform, Ammonia and Alkali Formate. Dilute acids have no action on it.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY. ER'S.	GOLD- CHL.	ACID PIC RIC.	DRAG.
103	Chloral Hydras	M. sub. c. distinctive o.	49-53	0.25	0.2	Nil.	Nil.	Nil.	Nil.
104	Chloramine —T.	Ac. Vap. odor of p-toluene sulph. chloride	De- comp.	7	Sol. c. de- comp.	Yell. col. folld. by pp.	Nil.	Yell. sol. gr. fluor.	Br. tarry pp.
105	Chloretone ...	Wh. sub. and irrit. vap.	80	200	1½	Nil.	Nil.	Nil.	Nil.
106	Chrysarobin (ACID CHRY- SOPHANIC)	M. ch. and yell. vap. bns.	152- 154	V. sl.	V. sl.	Nil.	Nil.	Nil.	Nil.
107	Cimicifugin...	Br. dist. vap. bns.	Nil.	Sl.	1	Nil.	Nil.	Nil.	Sl. br. pp.
108	Cinchonidine	M. ch. and alk. vap. bns.	202	V. sl.	20	Wh. pp.	Buff pp.	Yell. pp.	Red br. pp.
109	Cinchonine ...	M. ch. c. burnt feather odor vap. bns.	255	V. sl.	175	Wh. pp.	Buff pp.	Yell. pp.	Red br. pp.
110	Cinnamic Aldehyde	Evap. res. ch. vap. bns.	—	Sl.	Misc.	V. sl. pp.	Nil.	Nil.	Red br. pp.
111	Citric Acid vide ACID	—	—	—	—	—	—	—	—
112	Cocaine ...	M. c. yell. dist. ch. vap. bns.	98	Sl.	10	Wh. pp.	Buff. pp.	Yell. ppt.	Red br. pp.
113	Cocaine Hydrochlor	M. c. eff. to yell. liq. ch. and alk. vap. bns.	182 De- comp.	0.5	2½	Wh. pp.	Yell. pp.	Yell. pp.	Red br. pp.
114	Codeine Hydrochlor	M. to br. liq. c. eff. ch. br. dist. and vap. bns.	—	30	26	Wh. pp.	Lt.br. pp.	Yell. pp.	Red br. pp.
115	Colchicine ...	M. c. decomp. ch. alk. vap. bns.	143 De- comp. at 147	1	1	Sl. pp.	Buff pp.	V. sl. yell. pp.	Br. pp.
116	Colchicine Salicyl.	M. c. decomp. ch. alk. vap. bns.	55- 60	Sl.	1	Sl. pp.	Buff pp.	V. sl. yell. pp.	Br. pp.
117	Collargol ...	Br. sub. and alk. vap. bns.	Nil.	25	Insol.	Bl. pp.	Bl. pp.	Dark br. pp.	Or- ange pp.

No.	BROM. AQ.	SPECIAL TESTS.
103	Nil.	Compounds containing the group CX_3 ($X = Cl, Br, \text{ or } I$), on heating with 20% NaOH and Pyridine give a red col. which passes into Pyridine layer. Reaction detects less than 0.005 mgr. of Chloral Hydrate (<i>we found 0.00005 Gm.</i>) or Chloroform.—J.C.S. A. ii./24, 352. Warmed with a little strong NaOH solution, Chloroform is liberated. B.Pt. 94.4° — 96.7° C. 0.0001 Gm. c. NaOH and Aniline— <i>Carbylamine</i> .
104	Wh. pp.	Does not pp. or coagulate protein (distinction from Dichloramine T). Mixed c. eq. vol. Sat. aq. KI sol., Iodine is liberated. Gives wh. pp. with $HgCl_2$ sol. (Di-Chloramine does not give the latter).
105	Nil.	Gives Phenylisocyanide o. on warming c. Aniline and Caustic Potash solution. Iodoform is produced on shaking with Iodine and Aqueous Caustic Potash.
106	Nil.	Partially soluble in KOH sol. c. red colour. Allen gives tests to distinguish Chrysophanic Acid from Chrysarobin. (M.Pts. of commercial samples vary).
107	V. sl. pp.	General characters. No chemical test.
108	Yell. pp.	Gives neither Thalleioquin Test nor the $K_6Fe_2Cy_{12}$ Modification (<i>cf.</i> Cinchonine). Soluble in large amounts of Ether. Sodium Potassium Tartrate in neutral solution of a salt gives white precipitate. 0.0001 Gm. of Sulphate gives pp. c. Drag, Mayer's, etc.
109	Yell. pp.	Only slightly sol. in Ether (1 in 370). Few characteristic reactions. Not pptd. by $NaHCO_3$ in presence of Tartaric Acid (Quinine and Cinchondine are). Does not give Thalleioquin Test nor red col. with $K_6Fe_2Cy_{12}$ and Ammonia on addition of these to Acetic Acid soln. after treating with Br. (difference from Quinine and Quinidine). Not rendered fluorescent by very dilute H_2SO_4 .
110	Sol. floccy. pp.	B.Pt. 245 — 247° . May be oxidised into Benzaldehyde and Benzoic Acid.
111	—	—
112	Yell. pp.	<i>See Cocaine HCl.</i>
113	Yell. pp.	0.00001 Gm. pps. c. Mayer. 0.0001 Gm. c. Drag. Ac. Picric and Gold Chl. <i>See also Cocaine chptr.</i>
114	Yell. pp. rediss. at first.	0.0001 Gm. pps. c. Drag., Mayer & Gold. Does not reduce Iodic Acid (Morphine does). No blue colour with Ferricyanide and Ferric Chloride (Morphine gives) 0.001 Gm. warmed with 1 Cc. H_2SO_4 and 2 drops Fe_2Cl_6 soln. deep blue colour. Greenish-blue with Fröhde's Reagent.
115	Buff pp.	Only slightly sol. in Ether or Benzol. Practically insol. in Petrol Ether. H_2SO_4 with a trace of HNO_3 added gives yell.-gr. changing to blue vi. and wine red to yell. Cl water gives yellow pp. with an aq. Colchicine soln. sol. in NH_3 with or. col. $NaNO_2 + HCl$ give dirty br.
116	Buff pp.	Gives reactions of Colchicine and Salicylic Acid.
117	Yell. pp.	A substance having a black or metallic appearance and containing about 90% Silver.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC. RIC.	DRAG.
118	Coninæ HBr...	M. and evaps. c. br. dist.	214	2	3	Cream pp.	Or- ange red pp.	Nil.	Dark dirty red pp.
119	Cotarnin HCl.	Deep red and m., partly ch. and br. alk. vap. bns.	Abt. 125	Less than 0.5	3	Yell. pp.	Buff pp.	Yell. pp.	Red. br. pp.
120	Cotarnin Phthalas	M. to deep red liq. Ch. br. dist and alk. vap. bns.	Abt. 102	0.5	5	Cream pp.	Buff pp.	Yell. pp.	Red br. pp.
121	Coumarin ...	M. and evap. vap. bns.	67	Sl.	7	Nil.	Nil.	Nil.	Bl. resin- ous pp.
122	Cresylic Acid <i>vide</i> ACID	—	—	—	—	—	—	—	—
123	Cryogenin ...	M. ch. str. alk. vap. burns.	170	100	25	Nil.	Bl. br. pp.	Nil.	Br. yell. crysts from sl'wly.
124	Cubebin ...	M. ch. c. br. dist. and vap. bns.	128	V. sl.	Sl.	Nil.	Nil.	Nil.	Nil.
125	Dextrose (Com- mercial).	Ch. odor of burnt sugar, br. sub.	Nil.	Misc.	Sl.	Nil.	Nil.	Nil.	Nil.
126	Diacetyl- Morphine	M. then ch. alk. vap. burns.	169	800	44	Sl. wh. pp.	Sl. buff. pp.	Sl. yell. pp.	Red br. pp.
127	Diacetyl- Morphine HCl.	M. to br. liq. c. sl. eff. alk. vap. burns.	233	2½	13	Wh. pp.	Dirty yell. pp.	Yell. pp.	Red br. pp.
128	Dial... ...	Ac. vap. garlic odor.	170	Sl. Sol. cold, more hot.	Sl. Sol. cold, v. hot.	Cryst. pp.	Nil.	Yell. Cryst. pp.	Nil.
129	Di-Bromo Tannin Gelatin	Ch. c. nitro- genous odor.	Nil.	Almost insol.	Part. sol.	Nil.	Nil.	Nil.	Nil.

No.	BROM. AQ.	SPECIAL TESTS.
118	Yell. pp.	Conine with conc. H_2SO_4 gives a blood red turning gr. This liquid alkaloid is distinguished from Nicotine by giving no pp. with Platinic Chloride, and a deep red col. with Alc. soln. of Phenolphthalein. (<i>See also</i> Conium chapter.)
119	Yell. pp.	Hager says 0.3 Gm. dissolved in 4 to 5 Cc. water and Iodo-Potassic Iodide added, brown pp. formed which recrystallised from Alcohol melts sharply at $142^\circ C$. Cotarnin is dissolved in conc. Nitric Acid with a red colour and formation of Oxalic Acid.
120	Dark Yell. pp.	Decompose salt and identify the alkaloid and Phthalic Acid.
121	Deep Yell. pp.	Has a characteristic fragrant o. and sublimates at 100° . Dissolves slowly in hot NaOH sol. c. a slight gr. col., excess of acid reprecipitating Coumarin.
122	—	—
123	Nil.	The addition of 1 drop of Ferric Chloride to solution in conc. H_2SO_4 gives a deep red colour.
124	Nil.	With $K_2Mn_2O_8$ in alkaline solution oxidised to Piperonylic Acid and Oxalic Acid.—Schmidt.
125	Nil.	[α]D = $+104^\circ$ if pure in fresh sol. For the Hydrate [α]D = $+90$ to 96° . Aq. sols. of Silver are reduced when warmed. In addition to Fehling's, Barfoed's Reagent (warm) is also reduced (distinction from Dextrin and Maltose). Na, Ca and Ba Oxides form saccharates sol. in aq. Ferments c. Yeast (useful confirmatory test).
126	Yell. pp.	H_2SO_4 c. a little HNO_3 yellowish red, darkening on warming. From acid solns. is pptd. by Caustic Alkalis, Ammonia and Ammon. Carb. redissolved by the first in excess. Does not reduce Iodates (distinction from Morphine). <i>See also</i> HCl Salt.
127	Yell. pp.	0.0005 Gm. pps. c. Gold and Brom. Aq. Dissolve 0.05 Gm. in 5 Cc. water; add 3 drops Fe_2Cl_6 (5:100); no blue col. (Morphine). Nitric Acid dissolves c. yell. colour. Heat gently with care on v. small flame until it begins to turn green; remove from heat; it gradually assumes deeper coloration at edges. Morphine, Ethylmorphine and Codeine do not yield this reaction.
128	Nil.	0.001 Gm. After heating c. NaOH and acidifying with H_2SO_4 , CO_2 liberated with acetic odour. Millon's gives white pp. with a satd. sol., soluble in excess.—Cf. Malourea. Neither give pp. or colour with Nessler's Reagent, except after fusing with KOH.
129	Nil.	Gives violet with dilute NaOH.

No.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG
130	Di-Chloramine T.	M. then explodes odor of p. Toluene sulph. chlor.	De-comp.	Insol. almost.	Sol. c. de-comp.	Deep red.	Nil.	Yell. pp. gr. fl.	Nil.
131	Digitoxin ...	M. ch. yell. dist. vap. bns.	240	Insol.	140	Nil.	Nil.	Nil.	Nil.
132	Elaterin ...	M. yell. liq.	209	Insol.	160	Nil.	Nil.	Nil.	Nil.
133	Emetina ...	Part m. and ch. alk. vap. burns.	69	Sl.	3	Very sl. wh. pp.	Very sl. dirty cream pp.	Sl. yell. pp.	Dark red br. pp.
134	Emetine Bismuth Iodide	Bl.	—	Insol.	Insol.	Yell. pp.	Br. pp.	Yell. pp.	Br. pp.
135	Ephedrine HCl.	M. and gives arom. odor. ch.	215	7	8	Nil.	Nil.	Nil.	Red br. pp.
136	Ergotinine ...	Bl. c. part fusion.	Blk. at 210	Insol.	Sl.	Nil.	Nil.	Nil.	Nil.
137	Erythrol Nitrate.	M. and then ex. plodes.	61	Insol.	Abo't 90	Nil.	Nil.	Nil.	Nil.
138	Ethyl-Morphine HCl.	M. c. eff. and gives fish odor. ch. vap. burns.	124	10	25	Wh. pp.	Br. yell. pp.	Yell. pp.	Br. pp.
139	Eucaïn Lactate.	M. and evaps., vap. burns.	155	5	8	Wh. pp.	Cream pp.	Yell. pp.	Red br. pp.
140	Eucalyptol	Evaps. vap. burns and eucalyptus odor.	—	Sligh'y	Misc.	Nil.	Nil.	Nil.	Br. pp.

BROM. AQ.	SPECIAL TESTS.
Wh. pp.	Almost insol. in Aq. Pp. c. proteins. Sol. in Alc., Ether and Cotton Seed Oil, but decomposes them. Readily sol. in Chlorof. and Eucalyptus Oil without evident change. Dissolves in solutions of fixed alkalis forming the soluble Mono-chloramine. Strong oxidising agent, liberates Iodine from KI. Gives no pp. c. HgCl_2 (cf. Chloramine T).
Nil.	(See Digitalis this vol.), HCl Sp. Gr. 1.19 dissolves it cold s. color., but on warming it dissolves c. brown. col. <i>To 0.0001 Gm. in Petit's Liq. add 2 Cc. Acetic Acid and 1 drop 5% Fe_2Cl_6 and layer onto Conc. H_2SO_4 Br. ring and blue-gr. above.</i>
Nil.	With Fröhde's Reagent; first green then brown col. Mandelin's Reagent gives bl. A sol. of about 0.01 Gm. in 5 Cc. of melted Phenol becomes crimson, on adding a few drops of H_2SO_4 , changing to scarlet.
Sl. dark yell. pp.	Sulphomolybdic Acid gives brown colour changed to blue by HCl . <i>0.0001 Gm. in 5 Cc. Aq., pps. c. Drag, Mayer, etc.</i> <i>0.0002 Gm. e.g. in Ipecac. Wine gives yell. c. HCl and H_2O_2.—P.J. i./28,495.</i>
Br. pp. sol. in excess.	Gives reactions for Bismuth and Iodine. Quickly loses its red col. on shaking with Sodium Bicarbonate and (more slowly) with 0.2% HCl . Cf. Expts., Vol. I.
Yell. pp. rediss. & repp. by excess.	Ephedrine base melts at 38—40° and boils at 255° without decomposition. Pseudoephedrine base from another Ephedra variety melts at 117 to 118°.—Schmidt.
Nil.	Anhydrous Fe_2Cl_6 added to soln. in conc. H_2SO_4 gives yell. col. passing through or., crimson and gr. to a permanent blue. Dilute Acetic Acid layered on conc. H_2SO_4 gives an upper layer of vi. and a lower one of gr. at the junction.
Nil.	Liable to explode on percussion so that it usually occurs mixed with Milk Sugar or Oil.
Yell. pp. rediss. at first.	Does not give blue col. c. Fe_2Cl_6 or reduce Iodates direct. 0.01 Gm. dissolved in 10 Cc. H_2SO_4 , after liberation of the HCl , gives a clear sol., which on adding a drop of Fe_2Cl_6 sol. and warming turns violet to blue changing to red on adding 2 to 3 drops of HNO_3 . The free base is less soluble in NH_3 than Codeine . Such sol. re-pps. the base in crystals melting at 93° C. Dionine is distinguished from Morphine in that on adding it to $\text{K}_2\text{Fe}_2\text{Cl}_2\text{N}_{12}$ Sol. c. Fe_2Cl_6 , it does not give an immed. blue, but a bluish-green colour. <i>0.0001 Gm. in 5 Cc. Aq. gives wh. pp. c. Mayer.</i>
Wh. pp.	Eucaine Lactate and Eucaine Hydrochloride .—1 drop of 1% sol. mixed with 1 drop HgCl_2 sol. (1 in 20) gives no pp. (difference from Cocaine).—P. Helv. Latter also gives an Ammonia Precipitation Test in several stages, <i>q.v.</i> Not coloured by Fröhde's Reagent. 1 in 100 sol. gives no pp. with KI—distinction from Alpha-eucaine.— <i>B.P. '14.</i> Moistened with HNO_3 and evaptd. to dryness and Alcoholic KOH added—Benzoic Ether odour.—Hager. A 4% sol. of the Hydrochloride gives sl. golden br. pp. with Plat. Chlor. dissolving in HCl and throwing out again crystalline after a few mins.
V. sl. pp. rediss. at first.	1 Cc. in a freezing mixture, and eq. vol. of Phosphoric Acid added gradually; a solid white crystalline mass of Eucalyptol Phosphate results. If warm water be then added Eucalyptol will separate.—U.S. Agitated c. strong sol. of Iodine in Potassium Iodide a pasty mass is produced in which green lustrous crystals are formed.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. A.Q. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DR.
141	Euresol ...	Bright red nr. edge of liq. Acetic odor, vap. burns. and ch.	—	Sl.	Misc.	Nil.	Blu- ish. strks. come very sl'wly	Nil.	Re br pp
142	Eurobin ...	M. and ch. vap. burns.	Abt. 94	Pract. insol.	Sl.	Nil.	Nil.	Nil.	Nil.
143	Exalgine ...	M. and sub.	101	60	Free- ly.	Nil.	Nil.	Nil.	Br pp
144	Fluorescein	Part m. turns br. gr. ch. & swells up	—	Less than 1	2	Bl.	Yell. br. pp.	Yell. pp. redis.	Bl pp goe br.
145	Formalin ...	Boils,gives gas bns. blue, sl. res. ch.	—	Misc.	Misc.	Nil.	Nil.	Nil.	Nil.
146	Fuchsin ..	Part m. & br. vp. bns.	—	Slight	Abt. 20	Dark pp. pp.b. turns vi. pink.	Dark pp. sol. turns purple.	Br. pp. sol. yell.	Dar pp sol gr.
147	Gelseminine	M. ch. br. dist. and alk.vp.bns.	Abt. 178	Sl.	Sol.	Wh. pp.	Light br. pp.	Yell. pp.	Br pp
148	Glycogen ...	Ch. br. yell. vp. bns.	—	About 2 in- cmplte	Al- most insol.	Nil.	Nil.	Yell. pp.	Sl. red br.p
149	Guaiacol ...	Evap. c. charact. o. vp. bns.	Crysts. at 28°	Sl.	Misc.	Nil.	Nil pp.	Nil.	Br pp
150	Guaiacol Benzoas.	M. and evap., vp. bns.	50- 52	Alm'st insol.	50	Nil.	Nil.	Nil.	Nil.
151	Guaiacol Carbonas	M. & evaps. almost entirely vp. bns.	86	Nil.	Abt. 200	Nil.	Nil.	Nil.	Nil.
152	Guaiacol Cinnamas	M. to clear liq. goes br. c. yell.sub. & vp. bns.	130	Insol.	Sol.	Nil.	Nil.	Nil.	NI
153	Hexamine ...	Sub. s. m. or ch.	—	1	8	Nil.	Dirty yell.	Cryst. pp.	Br bl pp Nil
154	Hexyl- Resorcin	m. boils.	65	1700	Read- ily.	Nil.	Bl. pp.	Nil.	Nil.
155	Holocain HCl.	M. yell.ch. yel. dist. vp. bns. gr. flme.	186- 189	55	8	Wh. pp.	Buff. pp.	Yell. pp.	Br pp

BROM. AQ.	SPECIAL TESTS.
Yell. pp. rediss. at first.	Gives reactions of Resorcin and Acetic Acid. On cautiously heating 0.05 Gm. with 0.1 Gm. Tartaric Acid and 10 drops of H_2SO_4 a carmine red liquid is produced becoming pale yellow on diluting with water. On heating 0.1 Gm. with 2 Cc. N1 NaOH solution and a drop of Chloroform a crimson colour results, changed to yellow by a slight excess of HCl (Test for Resorcin, U.S.).
Nil.	This is an Acetyl derivative of Chrysarobin and usually has a slight odour of Acetic Acid. For general properties, v. Vol. I., p. 295.
Wh. pp.	Hydrolised to Acetic Acid and Monomethyl Aniline. Soluble 1 in 2 of Chloroform (differing from Acetanilide and Phenacetin).
Orange red pp.	Unmistakable fluorescence in alk. sol. Col. discharged by acid. Heated c. Zinc Dust and NaOH reduced to colourless Fluorescin.
Nil.	Adds NH_3 . Reduces Amm. Silver Nitrate sol. (Mirror). Responds to Schiff's Reagent. See also Milk Tests, Urine Tests and Paraform.
Almost bl. pp. floats, liq. decol.	Is decolorised by Zinc and HCl also by Sulphurous Acid. For detection of minute quantities as in urine, ext. with Acetic Ether or Amyl Alc. The color in these disappears both on adding NH_3 or HCl if Fuchsin present.
Yell. pp.	0.001 Gm. gives green col. with conc. Nitric Acid. 0.001 Gm. c. Sulphuric Acid and $K_2Cr_2O_7$, gives reddish-violet turning green.
Sl. wh. pp.	Iodine gives Burgundy red color. Readily soluble in alkalis. Dilute Acids convert it into glucose, but prior to that treatment does not reduce Fehling.
Dark orange pp.	B.Pt. 200-205° C. Characteristic odour and taste. An Alcoholic Solution with Ferric Chloride gives emerald-green colour changing blue and then brown.
Nil	Hydrolised gives reactions for Guaiacol and Benzoic Acid.
• Nil.	0.01 Gm. gives Guaiacol and Potassium Carbonate on hydrolysis with Alcoholic Potash.
Nil.	Hydrolised gives reactions for Guaiacol and Cinnamic Acid.
Yell. pp.	Boiled with dilute acids gives $HCOH$ and Ammon. Salt.
pp.	Paraffin odor on heating. H_2SO_4 cold dissolves; hot ch. and SO_3 . HNO_3 gives violent reaction.
Yell. pp.	Yellow waxy pp. with $NaNO_2$ and HCl.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ERS'.	GOLD CHL.	ACID PIC- RIC.	DR.
156	Homatropine	M. color- less, then ch. br. dist. alk. vap. burns.	98	V. sl.	Abt. 3	Wh. pp.	Buff. pp.	Nil.	Br.
157	Hydrastine ...	M. ch. alk. vp. bns.	132	V. sl.	150	Sl. cloud.	Nil.	Nil.	Sl. b. pp.
158	Hydrastinine HCl.	M. to yell. liq. ch. br. dist. vp. burns.	117	Less than 1	Abt. 5	Cr'am wh. pp.	Buff. pp.	Yell. pp.	Red br. pp.
159	Hyd. Succinas	Ch. and gives grey sub.	—	V. sl.	V. sl.	Yell. pp. turns red.	Nil.	Nil.	Nil. pp.
160	Hyd. Succini- midum.	Ch. grey sub. vap. burns sl. cyanide o.	—	28	V. sl.	Yell. pp. turns orange	Nil.	Nil.	Br. pp. turn ing crean Nil.
161	Hyd. Thymol- Acetas.	Ch. c. Ace- tic, then Thymol o. vp. bns.	—	Insol.	Sl.	Nil.	Nil.	Nil.	
162	Hyoscyne HBr.	M. ch br. dist & alk. v. bns.	—	3	14	Wh. pp.	Br. yell. pp.	Yell. pp.	Red br. pp.
163	Hyoscyamine Sulph.	M. ch. & alk. vp. bns	206	0.5	4	Wh. pp.	Yell. pp.	Yell. pp.	Red br. pp.
164	Hypnal. ...	M. c. Chloral odor ch. and give alk. and inflam. vap.	67—68	10	Abt. $\frac{1}{2}$	Sl. wh. cloud.	Buff. pp.	Yell. pp.	Br.
165	Indigo ...	Odor of HCN. Alk. vap. bns.	—	V. sl.	Insol.	Nil.	Nil.	Nil.	Nil.
166	Indigo-Car- mine.	Gives off water, nothing else charac- teristic.	—	100	Insol.	Deep blue pp.	Col. dis- charged slowly.	Nil.	Darl gr. pp.
167	Iodinol ...	I evolved.	—	Insol.	Insol.	—	—	—	—
168	Iohydrin ...	Br. c. oily dist. vi. vap. bns. and pun- gent res. ch.	—	Sl.	Misc.	Sl. wh. pp.	Sl. yell. pp.	Nil.	Br. pp.

No.	BROM. AQ.	SPECIAL TESTS.
56	Yell. pp.	Homatropine (HBr). — <i>Dilatation of pupil which passes off rapidly in comp. c. that prod. by Atropine. Does not react to Vitali's test (Ac. Nitric fuming, and Alcoholic KOH)—0.0001 Gm. gives yell. instead of violet given by Atropine, vide Atropine this chapter. Does not pp. c. Tannic Acid or Platinic Chlor. after adding HCl.</i>
57	Sl. cloud.	Fröhde's Reagent green to brown colour. Sulpho-Vanadic Acid gives orange red. To distinguish from Hydrastinine, see Hydrastis chptr. this vol.
58	Yell. pp.	The Sulphate dissolves with fluorescence. With Nessler's Reagent gives black pp. of Mercury.
59	Nil.	Practically insoluble in water but soluble in saline solutions—about 1 in 2 of 30% NaCl solution.
60	Nil.	Heated with alkali evolves Ammonia.
61	Nil.	Identify constituents, Thymol, Mercury and Acetate.
62	Yell. pp.	Response to Vitali's Reaction very similar to that with Hyoscyamine and Atropine. Gold Salt melts about 200° C.
63	Yell. pp.	Reaction with Vitali's Test (Fuming HNO ₃ and Alc. KOH) similar to that with Atropine, <i>q.v.</i> Gold Salt (recrystallised from hot aq.) is in golden shining leaflets, M.Pt. 160–163° C. Solns. reduce in the light. A 1 in 20 Soln. does not pp. c. Platinic Chor. sol.—difference from most alkaloids.—U.S.X.
64	Yell. pp. rediss. at first.	Reactions of Chloral and Antipyrin. Gives green pp. with NaNO ₂ and HCl.
65	Nil.	Purple vapours on heating in test-tube. Colour disappears on acting on it with Alkaline Reducing Agents, <i>e.g.</i> NaOH and Zinc.
66	Dark gr. pp. dissolving to br. sol.	General properties. Presence of Sodium Sulphite and Sulphate in ash. Diazo Test gives green colour.
67	Nil.	Oil evolving Iodine on heating.
68	Sl. Yell. pp. rediss. at first.	An oily liquid containing about 80% Iodine and having odour resembling Ethyl Iodide.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DR
169	Lævulose ...	M. to br. liq. c. cara- mel odor and ch. vap bns.	—	Less than 0.5	About 16	Nil.	Nil.	Nil.	NI
170	Lecithin ...	M. c. charac- teristic odor.	—	Sl.	30 misc. c. l. but throws out c. more.	Nil.	Nil.	Nil.	Or ang br pp
171	Luminal ...	Ac. vap. sm. of alc.	173	Al- most insol.	Sl. sol.	Col. cryst. pp.	Nil.	Yell. pp.	NI
172	Magisal ...	M., ch. odour of Phenol & Acetic Acid.	—	12	Insol.	Nil.	Nil.	Nil.	Yel pp.
173	Malachite Green.	Part. m. goes gr. up tube and then br. vap. burns.	—	2	Abt. 30	Dark gr. pp.	Dark gr. pp.	Dark gr. pp.	Dar dirt br. pp.
174	Malourea ...	M. and sub. en- tirely vap. bns.	191	150	9	Nil.	Nil.	Nil.	Nil.

	BROM. AQ.	SPECIAL TESTS.
9	Nil.	Reduces Bismuth salts in alkaline solution. On warming with KOH or NaOH turns brown (as also Glucose). Fermentable direct but more slowly than Glucose. Combines with Calcium Hydroxide forming insoluble gelatinous salt.
0	Dilute emulsion gives orange ppt.	Characteristic waxy appearance. Boiled with Baryta gives Glycerophosphoric Acid, Neurine and a fatty acid (Stearic, Oleic or Palmitic).—Watts.
1	0.1 Gm. in aq. 2 Cc. & 3 drops NaOH gives wh. cryst. ppt.	To distinguish from Veronal. Dissolve 0.1 Gm. in 1 Cc. H_2SO_4 c. heat and add 1 mgr. $NaNO_2$. Orange col. c. Luminal, none c. Veronal. After heating c. NaOH and acidifying c. H_2SO_4 , CO_2 evolved c. acetic sweet odour. Pp. c. Millon's, both before and after acidifying with HNO_3 , soluble in excess. Gives sl. col. c. Nessler. Mix 0.1 Gm. c. 0.5 Gm. KNO_3 , and 2 Cc. H_2SO_4 in a test-tube. Heat on boiling water-bath 10 mins. Pour into 10 Cc. of cold Aq. Reduce the ppt. Nitro comp. formed c. Zn. and decant the sol. Cool to $0^\circ C.$, acidify and add 0.1 Gm. KNO_3 in Aq. Add a portion of this to a sol. of <i>b</i> -Naphthol in Soda. Blood-red col. if Luminal. <i>Distinguishes between Barbituric Acid</i> c. or s. Phenyl, e.g. Luminal from Veronal.—J. Pharm. Chim., '25, 117, 69-70, per Analyst, '25, p. 465.
2	Wh. pp.	HCl precipitates Aspirin. The filtrate gives reaction for Mg. After hydrolysis gives the Fe_2O_3 salicylic acid reaction.
3	Dark gr. pp.	Its solubility in Amyl Alcohol distinguishes it from Methyl Green and its allies.
4	Nil.	Malourea, Syn., Veronal. —A satd. soln. acidified c. HNO_3 gives pp. c. Millon's, soluble in excess. This test is important. The M.Pt. is useful. Substance must be pure. Viscera (about 120 Gm.) are extd. c. Alc. and purified by Ether. 40 to 50% of the poison will probably have been excreted in the urine b. death. Note no pps. c. alkaloid reagents; not decomposed by boiling c. 20% NaOH; no br. col. c. Nessler, but after fusing with KOH, cooling and then adding Nessler, the usual br. col. A sol. treated c. 2 drops of Dilute HNO_3 and then c. Millon gives white pp. soluble in excess.—W. H. Willcox, L. ii./13, 1179. Ethyl Acetate instead of Ether good for extraction.—Y.B.P., 22, 157. According to our experiments (1921) c. Millon's.—Sat. aq. sols. <i>not</i> acidified with HNO_3 of Adalin, Bromural, Dial, Luminal, Malourea, Proponal, and Soneryl give pp. c. this Reagent, all sol. in excess, except that c. Adalin, which is not readily sol. If sat. sols. be first acidified c. a few drops of dilute HNO_3 , the same apply, but there is <i>no pp. with Adalin</i> . Acidifying Sodium Malourea (Medinal) of course throws out the Barbituric Acid. See also J.C.S., A. ii./25, 907. No pp. on addg. 8 Cc. Br. Aq. to 0.1 Gm. in 2 Cc. Aq. c. 3 drops NaOH. Luminal on the other hand pps.—Ph., Ned.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DR
175	Mannitol Nitrate.	M. goes br. and explodes.	113	Almost insol.	Sl.	Nil.	Nil.	Nil.	N
176	Medinal ...	Alk. vap. alc. and ammon. odor.	—	5	Almost insol.	Nil.	Nil.	Nil.	Bu PI
177	Mercurochrome	Chars.	—	Readily.	Insol.	Nil.	Purple col.	Nil.	Re PP
178	Methyl-Amino Oxybenzoas.	M. to Yell. liq. ch. br. dist. and alk. vap.	141	V. sl.	7	Nil.	Dark gr. pp.	Nil.	V. s. re br PP slow Ni
179	Methyl-Aspriodine	M. distills c. sl. dec'm.	40	Insol.	Misc.	Nil.	Nil.	Nil.	
180	Methyl-Atropin Nitras.	M. eff. ch. & br. dist. and alk. vap. burns.	149— 150	1	4	Wh. pp.	Cream pp.	Nil.	Du re PP
181	Methyl-Di-Tannin.	Ch. c. br. dist. Tannin odor.	—	Sl.	About 3	Nil.	Vi. col.	Nil.	Ni
182	Methylene Blue.	Swells and ch. sulphur odor.	—	About 6	Sl.	Copious blue pp.	Bl. pp.	Red bl. pp.	C pio bl
183	Migrainine and Migralgin.	M. then ch. and gives br. alk. vap. bns.	101— 105	0.8	1	Wh. pp.	Dull. yell. pp.	Bright yell. pp.	Or red pp
184	Morphine HCl.	Ch. c. br. dist.	—	24	About 55	Yell. wh. Gelatinous pp.	Yell. br. pp. turns darker	Yell. pp.	Red br. PP
185	Naphthol Bismuth.	Goes bl. c. red. br. sub.	—	V. sl.	Sl.	Nil.	Nil.	Nil.	Nil
186	Nicotine ...	Evaps. c. naus odor.	—	Misc.	Misc.	Wh. pp.	Buff pp.	Yell. pp.	Br. PP

No.	BROM. AQ.	SPECIAL TESTS.
75	Nil.	Explodes at 120° C.
76	Decol.	This, the Sodium Salt, gives the reactions characteristic of Veronal. Sol. 1 in 5 as against 1 in 145 for Veronal. On acidifying a sat. soln. the parent body is thrown out and can be identified. The Sodium may be titrated, using Phenolphthalein.
77	[Col. dis- charged.]	HCl precipitates dibromo-oxy mercury fluorescein. Heated c. H_2SO_4 and HNO_3 , cooled and diluted c. Aq., gives a pp. of HgS c. H_2S . Fused c. NaOH, dissolved in dil. HNO_3 , gives a pp. of $AgBr_2$ c. $AgNO_3$.
78	Dirty gr. br. pp.	Distinguished from Cocaine, Eucaïne, Stovaine, Holocaine, Novocaine, Alypin and Tropacocaine by Fröhde's Reagent, which gives a faint vi. tinge, but nothing c. the others, except Tropacocaine, which gives slight gr. Does not give Diazo reaction, but turns yell. c. $NaNO_2$ and HCl.
79	—	Fused c. NaOH, dissolved in dil. HNO_4 , gives pp. of AgI_2 c. $AgNO_3$. Heated c. conc. H_2SO_4 gives off vap. of Iodine.
80	Wh. pp.	Heated c. NaOH, Ac. Acetic added, soln. gives vi. col. c. Fe_2Cl_6 . Gives reactions of Atropine and a Nitrate.
81	Nil.	0.1 Gm. heated with 2 Cc. conc. H_2SO_4 gives a br. col. changing to gr. and then blue, and on adding Alcohol a blue turning to wine-red.
82	Bl. pp. and sol. almost color- less.	Slowly decolorised by reduction with Zinc and Acid. Alkali to aqueous solution changes colour to vi. Nitrous Acid converts into Methylene Green.
83	Yell. pp. rediss.	Give reactions of Phenazone and Caffeine. The Citric Acid present in Migrainine is not easily detected—solutions give no pp. with $CaCl_2$. The Phenazone may be pptd. c. Mayer (Caffeine is not pptd.). Caffeine yields the murexide reaction provided all the Phenazone pptd. c. Br. Aq. is filtered out first. If to a strong sol. of Migrainine or Migralgin Fe_2Cl_6 sol. be added in excess, then HCl, the red is destroyed and a Yel. pp. formed. Phenazone also gives this. Both give green colour and pp. with $NaNO_2$ and HCl. Migralgin dissolved in Aq., acidified c. HCl and shaken c. Ether, the Ether layer washed and extd. c. dilute alkali— Fe_2Cl_6 gives vi. col. of salicylate.
84	Yell. pp. at first.	Reddish vi. changing to slatey blue c. Fröhde's Reagent. Liberates Iodine from Iodic Acid. Gives blue pp. with Fe_2Cl_6 and $K_4Fe_2(CN)_{12}$ sol. (freshly prepared). To 0.00002 Gm. in 5 Cc. Aq. add a few Cc. H_2O_2 , then a few drops H_2O_2 and stir c. Copper Wire. Port Wine col.
85	Nil.	Hydrolysis gives Bismuth salt and β Naphthol.
86	Yell. pp. rediss. at first.	Liquid strongly alk. Dropped on paper, causes a grease spot which disappears after a time. Phosphomolybdic Acid gives greenish pp. Platin. Chlor. and Tannin also pp. in dilutions of 1 in 5,000 and 1 in 500 resp. Treated with a drop of $HCOH$ sol. and then HNO_3 —rose red col.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIO.	DRA
187	Nitrobenzene	Dist. ch. sl. vap. burns.	—	Sl.	1	Nil.	Nil.	Nil.	Ligh br. pp.
188	Novocain	M. to clear liq. ch. c. alk. vap. and naus. odor.	150	Less than 1	10	Wh. pp.	Br. pp.	Yell. pp.	Red. br. pp.
189	Nuclein ...	Ch. br. alk. vap. burns.	—	V. sl.	Insol.	Nil.	Nil.	Nil.	Nil.
190	Papaverine...	Alk. fishy vap.	147	Sl. Sol. hot ins'l.c.	Sl. Sol. hot V. Sl. c.	Wh. pp.	Buff pp.	Yell. pp.	Br. pp.
191	Paraform ...	Part m. and sub. vap. bns.	171	V. sl.	Sl.	Nil.	Nil.	Nil.	Nil.
192	Paraldehyde	Evaps. vap.bns.	10- 12	10	Misc.	Nil.	Nil.	Nil.	Nil.
193	Pelletierine (SOLID).	M. ch. and alk. burns.	46	4	3	Nil.	Nil.	Yell. pp.	Dark br. pp.
194	Petrol Ether	Evaps. vap. bns.	—	Insol.	4	Nil.	Nil.	Nil.	Nil.
195	Phenacetin...	M. and volatilises almost completely vap. bns.	135	Sl.	20	Nil.	Nil.	Nil.	Nil.
196	Phenalgine ...	Part m. and eff. dense sub. ch. alk. vap. burns.	—	Part.	Part.	Nil.	Sl. dark pp.	Nil.	Nil.
197	Phenazone ...	M. then ch. and br. vap. burns.	113	1½	1	Ppt.	Buff pp.	Yell. pp.	Red. br. pp.
198	Phenazoni Aceto- Salicylas.	M. Ace- tic then Phenol vap.	About 45	160	3½	Wh. pp.	Yell. pp.	Nil.	Red pp.

No.	BROM AQ.	SPECIAL TESTS.
187	Nil.	Detection of traces : distil with a little Sulphuric Acid in steam, shake distillate with Chloroform, convert oily drops into Aniline by reduction with Zinc and Sulphuric Acid.
188	Yell. pp. rediss. finally wh. pp.	Anhydrous base melts at 58—60°. <i>See also Cocaine Chapter.</i>
189	Nil.	<i>Cf. Acid Nucleinic.</i>
190	Yell. pp.	Fröhde's Reagent gives deep blue colour.
191	Nil.	Formalin odour on heating. Distillate in water reduces Silver Nitrate (forming mirror). Responds to Schiff's Test (Sulphurous Fuchsin solution). Na Nitroprusside 0.5% gives red which on acidifying c. Acetic Acid changes purple. Nessler's Reagent gives a reddish precipitate which gradually changes to grey. If to 5 Cc. H_2SO_4 in which 0.02 Gm. Salicylic Acid is dissolved, 2 drops of Formalin (37%) be added and the liquid gently warmed, a permanent red col. forms (U.S.). In general the reactions of Aldehydes.
192	Nil.	More soluble in cold water than hot—sat. aq. sol. becomes turbid on warming. Gives mirror with Ammoniacal Silver Nitrate on warming. Gives reactions of Aldehydes, but does not add Ammonia nor Sodium Bisulphite. Warmed c. H_2SO_4 it is converted into Acetaldehyde.
193	Wh. pp.	Gives deep blue pp. with Cobalt or Copper Sulphate. The base absorbs Oxygen from the air, resinifying.
194	Nil.	B.Pt. 50—60 °C. Does not dissolve Dragon's Blood (distinction from Benzol).
195	Nil.	$K_2Cr_2O_7$ in HCl soln. gives red col. 1 Cc. of a soln. of 0.2 Gm. in 2 Cc. HCl (25%) boiled, cooled and filtered gives reddish violet on adding 5 drops Cl water. Colour Reaction (Carletti).—Moisten a small quantity of Phenacetin in a dish c. Acetaldehyde, and 2—3 Cc. H_2SO_4 . On stirring with a rod the acid turns red (increased by warming). Delicate for 1 mgr. we found. The colour may be due to a condensation product; not given by Formaldehyde and distinguishes between these. Trioxymethylene and Hexamine do not give it.—C.D. ii./28,777.
196	Wh. pp. and eff.	Alcoholic extractive evaporated to dryness gives reactions of Acetanilide. Also contains Sodium Bicarbonate and Ammon. Carbonate.
197	Yell. pp. rediss.	Gives green pp. with HNO_3 . (Use Sodium Nitrite and a drop of H_2SO_4). Aq. sol. gives c. eq. vol. HNO_3 yell. soln. changing crimson on warming. Tannin gives a white pp. c. 1% solution. A drop of Fe_2Cl_6 sol. added to 2 Cc. of 1 in 1,000 sol.—red colour changing to yell. on adding H_2SO_4 . Estimate c. Picric Acid.—J. Rae, P.J. ii./28,575.
198	Wh. pp.	Gives reactions of Phenazone and Aspirin.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
199	Phenazoni Salicylas.	M. ch. br. dist. alk. vap.	90	200	4½	Wh. pp.	Sl. buff. pp.	V. sl. yell. pp.	Red br. pp.
200	Phenocoll HCl.	Part m. and ch. br. sub. alk. vap.	—	18	34	Wh. pp.	Nil.	Yell. pp. turns cryst.	Br. Red pp.
201	„ Salicyl ...	M. to br. liq. ch. alk. vap.	160— 165 De- comp.	Sl.	50	Nil.	Nil.	Yell. crysts form slwly	Br. red pp
202	Phenolph- thalein.	M. to br. liq. ch. Phenol o.	250	V. sl.	10	Nil.	Nil.	Nil.	Nil.
203	Phenoquin ...	Ch. Choking vap.	Abt. 210	Insol.	Sl. sol.	Nil.	Nil.	Nil.	Br. pp.
204	Phenyl- Aspirodine	m., boils, ch. iodine vap. phenol o.	123	Insol.	250	Nil.	Nil.	Nil.	Nil.
205	Phenyl- Sedasprin	m., boils, ch. HBr. & irrit. salicylic ac. odour	118	Insol.	380	Nil.	Nil.	Nil.	Nil.
206	Phloridzin ...	M. c. sl. eff. ch. and gives br. dist. and vp. bns.	107 solidi- fies & again m. 170	V. sl.	4½	Nil.	Nil.	Nil.	Nil.
207	Physostig- mine.	M. gives v. irritat- ing. vap. ch. alk. vp. bns.	75	Sl.	2	Wh. pp.	Br. pp. and pur- plish sol.	Yell. pp.	Red pp.
208	Physostig- mine Sulph.	M. gives irritating inflam. & alk. vap.	140	Less than 1.	Less than 2.	Wh. pp.	Fawn pp. turn- ing to bl. c. purple sol.	Yell. pp.	Red br. pp. turn- ing or.
209	Picrotoxin	M. ch. br. dist.	192	Sl.	13	Nil.	Nil.	Nil.	Nil.
210	Pilocarpine .	Boils, ch. & vp. bns.	—	V. easily.	Misc.	Wh. pp.	Crmy yell. pp.	Sl. yell. pp.	Br. red pp.
211	Pilocarpine Nitrate	Ch. alk. vp.	—	9	50	Wh. pp.	Crmy yell. pp.	Yell. pp.	Br. red pp.
212	Piperazin ...	M. & evaps vp. bns.	104— 107	2	3	Sl. wh. pp.	Red br. pp.	Sl. yell. pp.	Bl. to yell. pp.

No.	BROM. AQ.	SPECIAL TESTS.
199	Wh. pp.	Gives reactions of Phenazone and Salicylic Acid.
200	Yell. pp. rediss. first.	On treating 1 Cc. of sol. of 0.2 Gm. in 2 Cc. of HCl (25%) boiled, cooled and filtered, with 5 drops of fresh Cl water gives reddish vi. colour. 0.1 Gm. boiled with 2 Cc. 33% NaOH and then 2 drops of CHCl_3 added gives Isonitrile odour and bl. drops on surface.
201	Wh. pp.	Reactions of Phenocoll and Salicylic Acid.
202	Nil.	Red colour with Caustic Alkalis disappearing with acids. Silver Nitrate gives a violet pp.
203	Nil.	Sat. sol. in hot HCl gives pp. of brown crystals c. Pt. Chlor. Sol. Dissolve 1 Gm. in excess of Ammonia and evap. to dryness on w. b. or until free from NH_3 odour. Dilute c. water to 20 Cc. and filter. Separate portions of this give white pp. c. AgNO_3 sol., yell. pp. c. Lead Acet., and green pp. c. CuSO_4 .—U.S.X.
204	—	Fuse c. soda-lime, solve in aq., acidify c. HNO_3 and add AgNO_3 —yell. pp. <i>See also</i> Sedasprin.
205	—	Fuse c. soda-lime, solve in aq., add HNO_3 and AgNO_3 .—Yell. pp. Boil c. NaOH, cool, add Ac. Acetic and Fe_2Cl_6 . Violet col. produced.
206	Sl. Yell. pp.	Sols. have avidity for NH_3 . In taking up 10% it turns red and melts to a colourless mass. Mix 0.1 Gm. with a crystal of Vanillin and 1 drop of HCl conc. and warm—red col. results.
207	Yell. pp.	Calx Chlorinata turns a sol. red., but on further addition decolorises. It gives a brown col. c. NaNO_2 and HCl turning blue c. NaOH.
208	Yell. pp. rediss. at first.	Brown c. NaNO_2 and HCl, violet pp. with NaOH. If a salt is dissolved in Chloroform and heated to b.p. c. NaOH, the aq. layer becomes golden, while the Chlorof. is a pale rose.—J.C.S., A. ii./25,247.
209	Nil.	Mixed c. 3 x its weight of KNO_3 and moistened c. H_2SO_4 and then NaOH in excess added gives red.—Langley's Reaction. To a trace add 1 drop 20% Benzaldehyde in abs. Alc., then 1 drop H_2SO_4 s. shaking—violet (Melzer).
210	Pale Yell. pp. rediss. at first.	To a sol. in conc. H_2SO_4 add a trace of $\text{K}_2\text{Cr}_2\text{O}_7$.—Bluish-green changing to fairly permanent green. Phosphomolybdic Acid, Phospho-Tungstic Acid and Iodo-Potassic Iodide pp. from HCl solution.
211	pp. rediss. at first.	Dissolve 0.2 Gm. in 2 Cc. Aq., add 2 Cc. acidified H_2O_2 and small layer of Benzene. Add 4 drops 0.3% $\text{K}_2\text{Cr}_2\text{O}_7$ and shake. Aq. layer remains yellow—Benzene violet (distinction from other alkaloids).
212	Yell. pp. rediss.	Dissolves Uric Acid forming the neutral Urate. Piperazin Phosphate forms 4-sided tabular crystals. Gives white pp. with Nessler's Reagent.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
213	Piperazin Benz.	M.&evaps. vp. bns.	Abt. 167	100	10	Nil.	V.sl. buff pp.	Yell. pp.	Red br. pp.
214	Piperidine Tart.	M.vap.c. celery o.	Abt. 80	Less than 1.	About 30	Wh. crysts form	Nil.	Nil.	Br. pp.
215	Podophyllo- toxin	Part m. ch.br.dist. and vp.bns	117	V.sl.	Misc.	—	Nil.	Nil.	Nil.
216	Proflavine ...	Alk. vap. H ₂ S.	—	140	48	Or- ange. pp.	Deep gr. fluor.	Or- ange. pp.	Br. pp.
217	Preponal ...	Distills	145	Insol.	Sl.sol.	Nil.	Nil.	Nil.	Nil.
218	Pyramidon ...	Burns c. isonitrile odor.	108	20	2	Wh. pp.	Vi. col.	Yell. pp. rediss.	Br. pp.
219	Quinine ...	M. ch. c. br. dist. & alk.vp.bns.	172	V.sl.	1	Wh. pp.	Cre'm pp.	Yell. pp.	Br. red pp.
220	Quinine Sulphate	M. to red liq. ch. c. vi. then br. vap.	—	800	100	Wh. pp.	Cre'm pp.	Yell. pp.	Br. red pp.
221	Resorcin ...	M. & sub. vp. bns., c. sweet o.	110	1	0.5	Nil.	Grad. goes gr.	Nil.	Nil.
222	Saccharin ...	M. to clear liq. ch. wh. cryst. sub. & vp. bns. c. arom. o.	220	Sl.	25	Nil.	Nil.	Nil.	Nil.
223	Salacetol ...	M. and ch. vp. bns.	67	Sl.	14	Nil.	Nil.	Nil.	Nil.
224	Salicin ...	M. then ch. c. caramel odor.	198- 201	28	50	Sl. opal.	Nil.	Nil.	Nil.
225	Salicyl- Salicylas	M. gives wh. sub. ch. gives Phenol o. vp. bns.	142	Very sl.	15	Nil.	Nil.	Nil.	Nil.
226	Sal Limonis .	Ch. and sl. vap.	—	About 40	Sl.	Nil.	Nil.	Nil.	Br. pp.
227	Salocoll vide PHENOCOLL SALICYL.	—	—	—	—	—	—	—	—

NO.	BROM. AQ.	SPECIAL TESTS.
213	Yell. pp. rediss. at first.	Aq. sol. acidified c. HCl pps. Benzoic Acid. The aq. sol. gives test for Piperazin <i>q.v.</i>
214	Yell. pp.	Piperidine is a liquid with ammoniacal and peppery odour, and is a very strong base.
215	Nil.	Alkalies convert into gelatinous acid which loses water, giving a substance melting at 227°.
216	Buff pp.	Sols. are similar to those of Acriflavine. SO ₄ Reactions. Reduces Permanganate readily.
217	Nil.	After heating c. NaOH and acidifying c. H ₂ SO ₄ , CO ₂ evolved—pungent vapour c. odour resembling Menthol. Sat. sol. gives white pp. with Millon's— <i>cf.</i> Malourea. No colour with Nessler's Reagent except on fusing with KOH.—W. H. M., 1921.
218	Vi. col.	AgNO ₃ gives violet followed by pp. of Metallic Silver. Fe ₂ Cl ₆ gives bluish-violet. Violet with NaNO ₂ and HCl.
219	Yell. pp.	Dissolves c. blue fluorescence c. H ₂ SO ₄ , Acetic Acid and Tartaric Acid. White pp. c. NH ₃ soluble in Ether and in excess of NH ₃ . Thalleioquin Test with Cl and NH ₃ . Is distinctive for Quinine and shows less than 0.0001 Gm. Belladonna, Colchicum, Conium, Gelsemium, Ipecacuanha, Opium, Nux Vomica do not inhibit the reaction. Use dilute sols.
220	Yell. pp. rediss. at first.	<i>See reactions for Quinine.</i>
221	Yell. pp. rediss. at first.	On heating 0.05 Gm. with 0.1 Gm. Tartaric Acid and 10 drops conc. H ₂ SO ₄ carmine liquid forms which is yellow on diluting c. Aq. Not pptd. by neutral Lead Acetate (distinction from Pyrocatechin). Bluish violet with Fe ₂ Cl ₆ changing to yellow on adding NH ₃ ; distinction from Catechol and Quinol.—U.S. X. Resorcinol and Phloroglucinol are the only ordinary Phenolic compds. giving coloured pp. immed. in the cold when 2 Cc. of 40% Formaldehyde and 3 Cc. conc. HCl are added to a sol. of 0.1 Gm. in 3 Cc. 95% Alcohol.—J.C.S. A.I./24,638.
222	Nil.	<i>Dissolved in 25% KOH, q.s. and Br. Aq. added till yell., Br. substit. body is thrown out. 0.0001 Gm. heated c. 1 mgr. Resorcin and 1 drop H₂SO₄ yell., then dark green. After cooling dissolve in Aq. and add 1 or 2 drops 33% NaOH—intense fluorescence.</i>
223	Wh. pp.	Gives on alkaline hydrolysis reactions of Salicylic Acid and the liquid reduces Fehling's, smells of Meth. Salicyl. and burnt sugar and turns yell.
224	Nil.	Heated c. K ₂ Cr ₂ O ₇ , a few drops of H ₂ SO ₄ and some Aq. gives Salicylic Aldehyde (Meadow Sweet). Dissolves in HCl. and on boiling throws out Resin (Saliretin).
225	Sl. Yell.	Yields Salicylic Acid on hydrolysis. Formula C ₆ H ₄ .OHCOO. C ₆ H ₄ COOH, <i>i.e.</i> , Salicyl-Salicylic Acid.
226	Nil.	Calcium Chloride gives white pp. insoluble in Acetic Acid. Potash flame. Decolorises K ₂ Mn ₂ O ₈ with effervescence on warming at 60–65° with Acid Sulph. dil.
227	—	—

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
228	Salol ...	M. boils Phenol o.	43	V. sl.	10	Nil.	Nil.	Nil.	Nil.
229	Saloquinine	M. ch. alk. vp. bns.	139	V. sl.	120	Sl. opal- esce.	Nil.	Nil.	Sl. br. pp.
—	Salvarsan <i>see</i> (ARESNO BENZOL)	—	—	—	—	—	—	—	—
230	Santalol Salicylas.	Part evaps. c.	—	Pract. insol.	Abt.	Nil.	Nil.	Nil.	Nil.
231	Santonin ...	M. to clear liq. ch. gives br. dist.	170	Sl.	40	Nil.	Nil.	Nil.	Nil.
232	Sedasprin ...	M. ch. pung. o.	136	1500	4	Nil.	Nil.	Nil.	—
233	Sodii Cacodyl.	M. Bbl. sub.inflam. c. garlic o.	—	0·5	1	Nil.	Sl. buff.	Nil.	Red br. pp.
234	„ Glyceroph	Ch. and irrit. vp. bns.	—	0·35 slowly	Sl.	Nil.	Nil.	Nil.	Nil.
—	„ p-amino- phenyl Arsonas (<i>see</i> Arsamin)	—	—	—	—	—	—	—	—
235	„ Salicyl ...	Ch. c. odor of Phenol.	—	0·83	5½	Nil.	Nil.	Nil.	Nil.
236	Sodii Sulphocarb.	Decrepi- tates, ch. vap. bns. c. Phenol o.	—	5	150	Nil.	Nil.	Nil.	Nil.
237	„ Sulphori- cinas	Evaps. ch.	—	Misc.	Misc.	Nil.	Nil.	Nil.	Yell. br. pp.
238	Sodii Taurochelas.	Part m., swells up vp. bns.	—	0·5	About 2	Nil.	Nil.	Nil.	Br. resi- nous. pp.
239	Sparteine Sulph.	M. boils ch. Pyr- idinic o. vp. bns.	First at 62 and again 140	Less than 0·5	6	Wh. pp.	Buff. pp.	Yell. pp.	Red br. pp.
240	Stovaine ...	M. vola- tilises o. of varnish.	175	13	3	Wh. pp.	Yell. pp.	Yell. pp.	Buff. pp.
241	Strophanthin	Swells ch. c. br. dist. vp. bns.	Begins at 170 Com- ptly. at 190	Less than 1.	Abt. 1	Nil.	Nil.	Nil.	Nil.

No.	BROM. AQ.	SPECIAL TESTS.
28	Nil.	Alc. sol. pps. c. Bromine. Violet c. Fe_2Cl_6 in Alc. sol. Test for Phenol and Salicylic after melting c. soda, or heating c. Alc. KOH.
29	Nil.	On hydrolysis gives reactions of Quinine and Salicylic Acid.
30	Nil.	Alcoholic solution coloured violet by FeCl_3 .
31	Nil.	Warmed on w. b. c. 50% H_2SO_4 and a trace of FeCl_3 , yell. ccl. forms, then orange, red, violet and lavender, or a blood-red can be extd. by Amyl Alc. A crystal warmed c. Ethyl Nit. Sol. and a few drops of KOH gives a rose-red.
32	Nil.	Hydrolyse c. HCl., neutralise c. NaOH, add FeCl_3 —violet color. Fuse c. Soda Lime, solve and acidify c. HNO_3 , yell. ppt. c. HNO_3 .
33	Nil.	Few drops of aqueous solution with 2 Cc. Hypophosphorous Acid develop garlic odour of Cacodyl in a short time.
34	Nil.	On incineration, Pyrophosphate is formed. Lead Acetate precipitates but not Magnesia mixture. Cold Ammonium Molybdate, either precipitates on standing or heating.
235	Wh. pp.	See Acid Salicylic.
236	Decol- ourised	Dilute solution does not give yellowish brown with Uranium Nitrate (solution distinction from Salicylate), Soda flame. Incineration gives about 30% Na_2SO_4 .
237	Yell. pp.	Occurs as thick yellow liquid with characteristic odour.
238	Resin- ous greyish pp.	Taurocholic Acid forms shining hygroscopic bitter needles easily sol. in water and Alcohol. Solutions dextrorotatory. On heating at 100°C . or boiling with KOH or acids decomposes into Cholic Acid $\text{C}_{24}\text{H}_{40}\text{O}_5$ and Taurine $\text{C}_2\text{H}_7\text{NO}_3\text{S}$. To aq. sol. of the Na Salt add $\frac{2}{3}$ bulk of H_2SO_4 and a few drops of syrup—violet colour.—Pettenkofer's Bile Acid Test.
239	Yell. pp. rediss at first.	White pp. with CdI_2 . Sodium Phosphomolybdate gives white pp. soluble on heating. Ammon. Sulphydrate forms orange col. Grant's Test.—A strip of filter ppr. moistened c. the Chlorof. ext. of Ammoniacal solution of the alkaloid is dried and is exposed to Br. then to NH_3 fumes. On finally warming, a bright pink colour forms.—J.C.S. A. ii./25,448. <i>We found 0.0001 Gm. responds.</i>
240	Yell. pp.	Distinguished from Cocaine and other substitutes (except Holocaine) in that its aq. sol. gives pp. c. 10% Aqueous Ammonia, 10% KOH, and Sat. Sol. of Sod. Bicarb.
241	Nil.	Add a trace of Ferric Chloride and a few Cc. of concentrated Sulphuric Acid to an aqueous solution of Strophanthin 1 in 50. A pp. is formed which changes in two hours to dark green. Solutions are dextrorotatory.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG
242	Strychnine ...	M. to br. liq. & vp. bns.	268	V. sl.	150	Wh. pp.	Buff. pp.	Yell. pp.	Buff. pp.
243	Sucrose (CANE SUGAR)	M. yell. liq. ch. & vp. bns.	160	Less than 0·5	Abt 120	Nil.	Nil.	Nil.	Nil.
244	Sulphonah ...	Part m. cryst. sub. garlic vap.	126	Sl.	50	Nil.	Nil.	Nil.	Nil.
245	Terpineol (DISTILLATE FROM TERPINOL)	Evaps. ent'r'ly vp. bns.	—	Sl.	Misc.	Nil.	Nil.	Nil.	Br. pp.
246	Terpin Hydrate	M. evaps. inflam. sub.	116	Sl.	14	Nil.	Nil.	Nil.	Nil.
247	Tetrabrom- phenol- phthalein (SODIUM)	Coke like o. of Br.- phenol	—	Read- ily	Insol.	Nil.	Purp. Blue by refl. light	Crim- son	or. pp.
248	Tetra-iodo- phenol- phthalein (SODIUM)	Ch. Iod. vp.	—	Read- ily	Insol.	Nil.	Br. pp.	Nil.	—
249	Tetra-Iodo- Pyrrol.	B. & bl. sub. vi. vp.	—	V. sl.	21	Nil.	Nil.	Nil.	V. sl.
250	Theobromine	M. sub. res. ch. vp.	Abt. 300	V. sl.	Sl.	Nil.	Nil.	Nil.	Sl. res. br. pp.
251	Theobromine Aceto Salicyl	M. c. eff. to br. liq. wh. sub. ch. vap.	—	Sl.	Sl.	Nil.	Nil.	Nil.	Nil.
252	Theobromine Sodium Acetate	Part m. vp. wh. sub. chalk.	—	—	Sl.	Nil.	Nil.	Nil.	Yell. br. pp.

NO.	BROM. AQ.	SPECIAL TESTS.
242	Yell. pp.	Violet c. $K_2Cr_2O_7$ and H_2SO_4 , and yellow passing to violet c. Vitali's Reaction, v. Atropine, this chapter. Mandelin's Reagent gives blue colour changing to vermilion. On adding alkali pink to purple. Phosphomolybdic Acid will show 0.0001 Gm. Picric Acid 0.00005 Gm., Tannic Acid 0.00004 Gm. Mercuric Potassium Iodide 0.000006 Gm., Potassium Bismuth Iodide 0.00002 Gm., Platinic Chloride only 0.001 Gm., and Gold Chloride 0.0001 Gm.—Dragendorff.
243	Nil.	Conc. KOH turns this brown on heating . (Glucose is turned brown in the cold). Not directly fermentable—requires inversion by Yeast or dilute acids. Does not form Osazone or reduce Fehling's until hydrolysed. A mixture of 1 Cc. of Saturated Nickel Ammon. Sulph. sol., 1 Cc. of Sucrose sol. and few drops of H_2SO_4 or HCl is boiled when the green colour changes to yellow and then to red. 0.005 Gm. of Sucrose responds other sugars not interfering. Sucrose can be separated from a dry mixture with Dextrose by extraction with hot <i>Ethyl Acetate</i> , <i>Sucrose being insoluble</i> .
244	Nil.	By fusion c. KOH, a red becoming blue on diln. c. Aq. is produced and S. is pptd. on acidifying. Heated c. Charcoal, Mercaptan is evolved.
245	Nil.	Strong odour of Hyacinths and Lilac. B.Pt. 215–218° C. See Vol. I., p. 804.
246	Nil.	On adding few drops conc. H_2SO_4 to hot solution the liquid becomes turbid and odour of Lilac produced.
247	Yell. pp.	Fused c. NaOH dissolved in HNO_3 pp. of AgBr c. $AgNO_3$. The phthalein compd. is pptd. as light buff pp. c. acid.
248	Yell. pp.	Wh. pp. c. HCl. which rediss. in NaOH c. return of blue col. Fuse c. NaOH. Add HNO_3 and $AgNO_3$ —yell. pp.
249	Nil.	Warmed c. NaOH and Zn., fumes of Pyrrol are given off. These colour Pine Wood, e.g., a match, soaked in HCl red. Gives red on warming an Alc. sol. c. HNO_3 .
250	Nil.	Gives Murexide Test. Pps. Silver Theobromine on adding $AgNO_3$ sol. to a very dilute sol. of the Nitrate. Sodium Phosphotungstate gives yellow pp. Heated c. dil. H_2SO_4 and Lead Dioxide (avoiding excess), CO_2 is evolved. The product pps. S. from H_2S , colours skin purple and turns blue a little Magnesia.
251	Nil.	Reactions of Theobromine and Aspirin.
252	Nil.	Gives Murexide Reaction. Aqueous solution 1 in 5 neutralised with dilute Hydrochloric Acid in presence of Litmus solution gives white precipitate of Theobromine. (A little alkali assists its solubility in water).

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (lin—)	SOL. ALC. (lin—)	MAY- ER'S.	GOLD CHL.	ACID PIC RIC.	DRAG.
253	Theobromin- Sod-Salicyl	Ch. Phenol odor wh. dist. vap.	—	2 (cf. Vol.I.)	V. sl.	Nil.	Br. color & v. sl pp.	Nil.	Deep br. pp. turn- ing light- er.
254	Theophylline.	M. to yell. liq. sub. res. ch. vap.	266	Sl.	90	Nil.	Nil.	Nil.	Br. bl. pp.
255	Theophylline Sodium Acetate.	Part. m. and ch. vap.	—	20	Sl.	Nil.	Br. col.	Nil.	Dark br. pp.
256	Thioresorcin	Ch. yell. sub. and vap.	—	V. sl.	V. sl.	Nil.	Nil.	Nil.	Nil.
257	Thiosinamin	M. to liq. garlic od. ch. alk. vap.	74	18	2	Wh. pp.	Buff. pp. rediss.	Nil. at first sl. pp. a.	Or. yell. pp.
258	Thiosinamine Ethyl Iodide	Ch. alk. vap. garlic	68	Easily.	Misc.	Wh. pp.	Br. bl. pp.	Yell. pp.	Red- br. pp.
259	Thymol	M. evaps. aromatic vap.	50- 51	1500	0.37	Nil.	Nil.	Nil.	Nil.
260	Thymol Iodide	M. to br. c. vi. br. vap.	Nil.	Insol.	V. sl.	Nil.	Nil.	Nil.	Nil.
261	Toluol ...	Evaps. entirely vap.	—	V. sl.	1	Nil.	Nil.	Nil.	Nil.
262	Tribrom- phenol.	M. ch. wh. sub. irritat- ing vap.	85	Insol.	3	Nil.	Nil.	Nil.	Nil.
263	Tribrom- phenol Bismuth.	Bl. and gives yell. sub. first and br. a.	—	Insol.	Insol.	Nil.	Nil.	Nil.	Nil.
264	Trional ...	M. boils ch. odour of mer- captan.	76	420	11	Nil.	Nil.	Nil.	Nil.
265	Tropacocaine HCl.	M. ch. br. sub.	—	2	About 9	Wh. pp.	Yell. pp.	Yell. pp.	Red. pp.

NO.	BROM. AQ.	SPECIAL TESTS.
253	Wh. pp. rediss. at first.	On acidifying c. HCl Salicylic Acid is thrown out. Remove Theobromine from the filtrate c. Chloro., this gives Murexide Reaction.
254	Cryst. pp. Nil. first.	Gives Murexide Reaction.
255	Red-br. c. excess Reagent.	Gives reactions of Theophylline and also of Acetate (after removing the Theophylline by neutralising and filtering).
256	Nil.	Yellow powder. Oxidation gives a Sulphonic Acid.
257	Yell. pp. rediss. opales- cence.	Usually has a faint garlic odour. Heated with Lead Hydroxide, Hydrogen Sulphide is removed.
258	Br. pp.	Usually has slight garlic odour. NaNO ₂ and HCl gives brown pp. Yellow pp. with Lead Acetate insoluble in dilute HNO ₃ but blackened by conc. HNO ₃ .
259	Wh. pp.	Characteristic odour, <i>see</i> Vol. I., p. 809. B.Pt. 232° C.
260	Nil.	Iodine evolved on heating with H ₂ SO ₄ .
261	Nil.	B.Pt. 109—111° C. On oxidation yields Benzoic Acid.
262	Nil.	Characteristic odour.
263	Nil.	Decomposed by acids, giving Bismuth Salt and Tribromphenol (M.Pt. 85°).
264	Nil.	Heated c. charcoal gives mercaptan odour.
265	Yell. pp.	Boiled with HCl, this is converted into Benzoic Acid and Pseudo-tropine.

NO.	SUBSTANCE.	HEAT.	M.PT. °C.	SOL. AQ. (1in—)	SOL. ALC. (1in—)	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
266	Tylcalsin ...	M. ch. odour of Phenol & Salicyl. Esters.	—	6	—	Nil.	Nil.	Nil.	Yell. pp.
267	Tyllithin ...	M. ch. odour of Phenol & Salicyl. Esters.	—	1	4	Nil.	Nil.	Nil.	Yell. pp.
268	Tylmarin ...	M. ch. odor vap.	152	Sl.	15	{Nil.	Nil.	Nil.	Nil.
269	Urea... ..	M. gives wh. sub. and vap. Res. solid then sub.	132	1	7½	Nil.	Nil.	Nil.	Nil.
270	Urethane ...	M. evaps. vap.	50	2	Less than 1	Nil.	Nil.	Nil.	Nil.
271	Veratrina ...	M. to yell. br. liq. br. dist. vap.	145- 155	V. sl.	3 .	V. sl. wh. pp.	Sl. cloud	Nil.	Red br. pp.
	Veronal see Malourea								
272	Yohimbin ... HCl	M. to br. liq. beastly odor. ch. vaps.	300	Sl.	100	Wh. pp.	—	Yell. pp.	Red br. pp.
273	Zinc Sulpho- Carb.	Ch. c. odor of Phenol. vap.	—	2	3½	Nil.	Nil.	Nil.	Nil.

No.	BROM. AQ.	SPECIAL TESTS.
266	Wh. pp.	HCl precipitates Aspirin. The filtrate gives reactions for Ca. After hydrolysis gives reactions for Salicylic Ac.
267	Wh. pp.	As above for Tylcalsin except filtrate gives reactions for Li.
268	Sl. cloud.	Soluble 1 in 14 in Chlorof. (Acid Coumaric is only slightly soluble). Hydrolised by alkali giving Acetate and Coumarate.
269	Nil.	Heated, gives NH_3 and residue gives Biuret Test. Urea Nitrate pptd. from strong sols. Decomps. c. Hypobromite (<i>see also</i> Urine Anal. Chapter).
270	Nil.	Heated with KOH, it yields NH_3 , K_2CO_3 and Alcohol.
271	Yell. pp.	Mixed with powdered Cane Sugar and H_2SO_4 it gives green colour turning blue. Heated with HCl on water bath a blood-red solution obtained.
272	Nil.	The solid and sols. of the base turn orange on exposure. Becomes deep green and then yellowish c. Conc. HNO_3 , changing to cherry-red c. Alc. KOH. Ammoniacal Silver Nitrate is reduced by it.
273	Decol- orised.	Yellowish green pp. with Pot. Ferro-cyanide, insoluble in HCl (method of distinction of Zinc from Aluminium in analysis).

Approximate Melting Points and Consistence (*Atmospheric Temperature, 11° C*) of some Fats and Waxes suitable for Suppositories, Pastes, Creams, and Ointments.

	31-32° C	37.8-89.6° F.	
Oleum Theobromatis			Yellowish white, hard, brittle, and melts with ease.
Sevum Præparatum	39	102.2	Rather hard and brittle, but melts with ease
Oleum Theobromatis			{ Stiff paste. Easily softened with the fingers. Suitable for thick creams.
Paraffinum Molle	33-34	91.4-93.2	
Oleum Theobromatis			White, soft base.
Paraffinum Molle	35-39	95-102.2	Soft, white, unctuous.
Unguentum Cetacei, (B.P.'14)	35	95	Hard, tough, and tenacious, tallowy. Obtained from <i>Rhus</i> species.
Adeps	38	100.4	Yellowish, stiff, tenacious, unctuous.
Japan Wax	50	122	{ Hard. Melts easily between the fingers. Not so brittle as Oleum Theobromatis.
Adeps Lanæ	40-44	104-111.2	
Oleum Theobromatis			Soft and unctuous.
Cetaceum	39-40	102.2-104	Crystalline, scaly and slippery.
Sevum Præparatum	47	116.6	Stiff unguent.
Cetaceum	46-50	114.8-122	Very hard white mass.
Unguentum Paraffini, (B.P.'14)	47	116.6	
Ceresin	52	125.6	
Stearin			
Cera Alba 1, Oleum Theobromatis 6	51-52	123.8-125.6	Hard glossy mass. Easily melts between the fingers
Japan Wax, Hard Paraffin, equal parts	48-51	118.4-123.8	Hard, white and brittle.
Ceresin	52-53	125.6-127.4	Hard, like good paraffin.
Stearin	53-54	127.4-129.2	White, hard, crumbling substance.
Paraffinum Durum	54-57	129.2-134.6	{ Crystalline, hard and unctuous (slightly greasy).
Unguentum Resinæ, B.P.'14	54	129.2	
Adeps 3 with Cera Alba 1	59	138.2	Stiff white pomade.
Adeps, Cera Alba, equal parts	58	136.4	Very hard, white mass.
Cetaceum, Cera Alba, equal parts	58-59	136.4-138.2	Hard as last, but not so white in appearance.
Cera Alba	62-64	143.6-147.2	White, hard, tenacious.
Carnauba Wax	85	185	Hard, yellowish, from leaf buds of <i>Copernicus cerifera</i> (a palm growing in Brazil).
Carnauba Wax 1, Oleum Amygdalæ 4	77-78	170.6-172.4	Stiff mass, melting easily.
Carnauba Wax 1, Oleum Amygdalæ 3	78-79	172.4-174.9	Stiff ointment of brownish colour.
Cera Alba, Oleum Amygdalæ, eq. pts.	60-61	140-141.8	Hard and wax-like.
Cera Alba 1, Oleum Amygdalæ 5	54	129.2	Stiff ointment.
Cera Alba 1, Oleum Amygdalæ 9	52-53	125.6-127.4	Stiff ointment base.
Cera Alba 1, Oleum Amygdalæ 19	48-49	118.4-120.2	{ Very soft creams
Cera Alba 1, Oleum Amygdalæ 39	43	109.4	

FREEZING MIXTURES.

For cooling and setting suppositories, bougies, &c.

The following is a list of some freezing mixtures best prepared from commercial Crystalline Salts and in a thick wooden vessel :—

	Temp. F reached.
Ammonium Nitrate 1, Water 1	+ 1.4
Sodium Nitrate 3, Dilute Nitric Acid 2	— 3
Ice 2, Sodium Chloride 1	— 5
Ammonium Nitrate 1, Sodium Carbonate 1, Water 1	— 7
Ice 24, Sodium Chloride 5, Ammonium Nitrate 5	— 18
Ice 3, Sulphuric Acid 2	— 23
Ice 8, Hydrochloric Acid 5	— 27
Ice 3, Dilute Nitric Acid 2	— 46
Ice 8, Dilute Sulphuric Acid 10	— 91

SULPHURIC ACID, Sp. Gr. and PERCENTAGE TABLE, u/u .

Sp. Gr.	%	Sp. Gr.	%	Sp. Gr.	%	Sp. Gr.	%	Sp. Gr.	%
1.020	3.03	1.165	22.83	1.330	42.66	1.530	62.53	1.760	82.44
1.035	5.23	1.185	25.4	1.355	45.35	1.560	65.08	1.785	85.10
1.055	8.07	1.200	27.32	1.380	48.00	1.590	67.58	1.805	87.6
1.070	10.19	1.220	29.84	1.400	50.11	1.620	70.32	1.820	90.05
1.085	12.3	1.240	32.28	1.425	52.03	1.645	72.4	1.832	92.52
1.105	15.03	1.265	35.14	1.450	55.03	1.675	74.97	1.839	95.00
1.120	17.01	1.285	37.45	1.480	57.83	1.705	77.60	1.842	97.70
1.145	20.26	1.305	39.77	1.505	60.18	1.735	80.24	1.8385	99.95

HYDROCHLORIC ACID, Sp. Gr. and PERCENTAGE TABLE, u/u .

1.010	2.14	1.060	12.19	1.105	20.97	1.145	28.61	1.185	36.31
1.025	5.15	1.070	14.17	1.115	22.86	1.155	30.55	1.190	37.23
1.040	8.16	1.080	16.15	1.125	24.78	1.165	32.49	1.195	38.16
1.050	10.17	1.090	18.11	1.135	26.70	1.175	34.42	1.200	39.11

NITRIC ACID, Sp. Gr. and PERCENTAGE TABLE, u/u .

1.020	3.70	1.150	24.84	1.280	44.41	1.390	63.23	1.465	81.42
1.040	7.26	1.170	27.88	1.305	48.26	1.405	66.40	1.475	84.45
1.060	10.63	1.185	30.13	1.325	51.53	1.420	69.80	1.485	87.70
1.085	13.95	1.210	33.82	1.345	54.93	1.430	72.17	1.495	91.60
1.100	17.11	1.235	37.53	1.360	57.57	1.445	75.98	1.505	96.39
1.125	21.00	1.260	41.34	1.375	60.30	1.455	78.60	1.520	99.67

POTASSIUM HYDRATE, Sp. Gr. and PERCENTAGE TABLE, u/u .

1.014	1.7	1.108	12.9	1.220	24.2	1.357	35.9	1.530	49.4
1.029	3.5	1.125	14.8	1.241	26.1	1.383	37.8	1.563	51.9
1.045	5.6	1.142	16.5	1.263	28.0	1.410	39.9	1.580	53.2
1.060	7.4	1.162	18.6	1.285	29.8	1.438	42.1	1.597	54.5
1.075	9.2	1.180	20.5	1.303	31.8	1.468	44.6	1.615	55.9
1.091	10.9	1.200	22.4	1.332	33.7	1.498	47.1	1.634	57.5

SODIUM HYDRATE, Sp. Gr. and PERCENTAGE TABLE, u/u .

1.014	1.20	1.125	10.97	1.252	22.64	1.345	31.22	1.438	39.99
1.029	2.71	1.142	12.64	1.274	24.81	1.357	32.47	1.453	41.41
1.045	4.00	1.162	14.37	1.285	25.80	1.370	33.69	1.468	42.83
1.060	5.29	1.180	15.91	1.297	26.83	1.383	34.96	1.483	44.38
1.075	6.55	1.190	16.77	1.308	27.80	1.397	36.25	1.498	46.15
1.091	8.00	1.210	18.58	1.320	28.83	1.410	37.47	1.514	47.60
1.108	9.42	1.231	20.59	1.332	29.93	1.424	38.80	1.530	49.02

DROP MEASURE TABLE.

Showing the number of drops per gramme of various medicaments delivered (at 15° C.) by a standard pipette 3 mm. in external diameter. Adapted from F.E.

	No. of drops in 1 Gm.
Acetum Opii Compositum.. .. .	54
Acidum Hydrochloricum (1·171)	21
„ Hydrocyanicum Dilutum (2%).. .. .	22
„ Nitricum, Sp. Gr. 1·321	25
„ Phosphoricum, Sp. Gr. 1·35 (50% H_3PO_4)	19
„ Sulphuricum, Sp. Gr. 1·843	26
„ Sulphuricum Alcoholisatum (Aqua Rabeliana) (Sulphuric Acid 1, Alcohol 3) (cautiously mixed)	55
„ Sulphuricum Dilutum 10%	21
Æther	19
„ Aceticus, Sp. Gr. 0·915	60
„ Sulphuricus Alcoholisatus (Hoffman's Anodyne) Ether 4 and Alcohol 1, mixed)	73
Aqua Distillata	20
Chloroformum, Sp. Gr. 1·48	60
Creosotum, Sp. Gr. 1·08	42
Liquor Ammoniae, Sp. Gr. 0·923	24
Oleum Crotonis Tiglii (Aceite de Croton Tiglio)	44
„ Menthae Piperitæ, Sp. Gr. 0·89 to 0·92	52
„ Terebinthinæ	56
Solutum Chloruri Ferri, Sp. Gr. 1·26 (Liquor Ferri Perchloridi)	18
Tinctura Alcoholica Aconiti (1 of Root in 10)	58
„ „ Belladonnæ, 1 in 10	59
„ „ Cantharidis, 1 in 10 (with Cochineal 1·5 in 100)	58
„ „ Castorei, 1 in 20	57
„ „ Colchici, 1 in 10	59
„ „ Corticis Aurantii (Naranja) Composita (Tinctura Roborans ex Whytt)	63
„ „ Digitalis, 1 in 10	58
„ „ Fabæ Sancti (Haba de San Ignacio) (Ignatii Composita) Guttæ Amaræ ex Baumé 1 in 2	58
„ „ Hamamelidis (bark and leaves of each, 1 in 20)	58
„ „ Hydrastis, 1 in 10	58
„ „ Iodi (1 in 10, Alcohol 95%) (Solution Alcoholica de Yodo)	62
„ „ Lobeliæ, 1 in 10	58
„ „ Moschi (Almizcle) 1 in 25	55
„ „ Nucis Vomicae, 1 in 10, 0·25% Alkaloids approximately	57
„ „ Opii Extract, 1 in 20	58
„ „ Scillæ (escila) 1 in 5	58
„ „ Strophanthi (Estrofanto) 1 in 10	58
„ „ Viburni, 1 in 10	58
(all the above tinctures are made with Alcohol 70%).	
Vinum Opii Compositum (Laudanum ex Sydenham)	40

NUMBER OF DROPS PER CUBIC CENTIMETRE OF B.P. 14 PREPARATIONS, DELIVERED BY A 3 mm. PIPETTE AT 22°C.

Acid Carbolicum Liquidum	35·0
Acid Hydrocyanicum Dilutum	16·5
Aqua Destillata	17·5
Chloroformum	75·0
Creosotum	34·0
Extractum Ipecacuanhæ Liquidum	50·0
Liquor Arsenicalis	20·0
Liquor Plumbi Subacetatis Fortis	20·0
Liquor Strychninæ	35·0
Oleum Cinnamoni	34·0
Oleum Menthae Piperitæ	37·0
Tinctura Capsici	47·0
Tinctura Strophanthi	45·0

SYNTHETIC NOTES.

Physiological effect in comparison with Chemical constitution of Drugs.

There are various theories of the action of Poisons on the cell elements of the body. That of *Ehrlich* suggested that the poison becomes attached to the tissues by various chains or anchors before the poisoning can take place. The theory maintains that when these chains or groups become somewhat altered the union takes place with another cell structure, hence causing a different result.

The theory of *Loew* holds that substances which *can act on Aldehyde or Amino-groups* must be poisons to living tissues—they will act by substitution. According to him the greater the reactivity the greater the physiological result, *e.g.*, *Phenylhydrazine* and *Hydroxylamine* are very reactive to Ketone and Aldehyde groups,—hence poisonous both to plants and animals. *Aniline* is less reactive to Aldehydes than *Phenylhydrazine* and is less poisonous than the latter. If the chemical properties of a poison are *made more labile* by a change in the character of the molecule, then it becomes *more toxic* and *vice versa*, *e.g.*, if the Hydrogen of the NH group in many alkaloids be replaced by a Methyl group the toxicity is diminished as the substance reacts less readily with Aldehydes. Similarly *Piperidine* is more toxic than *Pyridine* and *Tetra-hydroquinoline* is far more toxic than *Quinoline* by reason of the fact that the reduced Compounds which contain secondary Nitrogen in place of tertiary have a greater reactivity with protoplasm. Compare also *Pyrogallol* (*Trihydroxybenzene*) which is more poisonous than *Dihydroxybenzene* (*Catechol*) and *Phenol*. The toxicity of Phenols is in the light of this theory attributed to their reactivity,—especially with Aldehyde. *Salicylic Acid* (introduction of COOH) is less reactive with Aldehydes than *Phenol*, hence less toxic. *Loew's Theory only applies to certain bodies reacting with Aldehyde and Amino groups*, it does not explain selective action. Every tissue contains labile Aldehyde and Amino groups,—hence should react with a drug.

Reverting to *Ehrlich's Theory*,—in the example of *Morphine* it is thought that one of the anchors may be one of the OH groups. If these are combined with H_2SO_4 (forming *Morphine-Sulphuric Acid*) the substance cannot attach itself to nerve tissue, hence *Morphine-Sulphuric Acid* has no hypnotic effect. (Another explanation of this may be purely physical—the compound is far less soluble). The entrance of an organic radicle—Methyl, Ethyl, Acetyl causes the hypnotic power to be reduced whilst action on the respiratory centres (produced by *Morphine* to a slight extent) is much increased, *e.g.*, in the case of *Codaine* and *Diacetyl Morphine*.

The relationship between *Arecoline* (the Methyl Ester of *Arecaidine*) and *Arecaidine* exemplifies the fact that in cases where the presence of an Acid group prevents the substance from acting physiologically in spite of the presence of an anchoring group, the conversion of the acid into an Ester causes the physiological action to appear. The Methyl group in this case does not cause

the marked difference,—the effect resides in the Arecaidine which is prevented from showing itself by the Acid group present,—*cf.*, also Benzoyl-Ecgonine and its Methyl Ester which is Cocaine. Note that analogous effects can be brought about by Ethyl as by the Methyl group. When the Carboxyl group in the molecule is masked we get anæsthetic effect.

With regard to the question of physiological action depending on chemical change of the substances while passing through the organism, a few observations may be offered between some closely related compounds. Wide generalisations cannot be made in these questions,—a case to illustrate this is the decomposition of Xanthine, Theobromine and Caffeine, the first being without action on the heart muscle, the second acting slightly and the third showing more marked toxic action. It was found that the products of metabolism after giving Caffeine and Theobromine contain Xanthine bases poorer in Methyl groups than the substances given,—the Methyl groups had been split off. In man Caffeine is reduced to Theophylline,—this shows that there is a *splitting off of Methyl groups* which groups appear to be responsible for action on the heart, *i.e.*, there is a relationship between physiological action and the changes undergone by the substance in the organism. It is, therefore, often useful in devising new Synthetic Drugs to determine the substances that are formed in the organism when an unsuitable substance is administered. Aniline, for example, is eliminated as Para-amino-phenol,—this led to the introduction of a number of derivatives of this substance of which *Phenacetin* is the best known example. We shall revert to the question of alterations that take place in drugs passing through the system later.

Alkaloids in general seem to pass through the system for the most part *unaltered* and their action is hence difficult to explain. If a substance is easily acted upon it will react *with all tissues* and hence produce no specific effect. (Hydrocyanic Acid can only be given in small doses for this reason.)

Whilst mentioning Alkaloids we should add the classic discovery of Crum Brown and Fraser. They showed that various Alkaloids possessing the most diverse physiological actions on combination with Alkyl halides to form quaternary Ammonium derivatives,



where $\text{R}_1\text{R}_2\text{R}_3$ are Organic Radicles of any complexity and RX stands for Alkyl halide, Methyl or Ethyl Iodide, etc., yield substances in almost every case possessing the property of paralysing the motor-nerve endings in the same way as Curare. One can obtain therefore by *Methylation* from all tertiary bases, quaternary Ammonium Compounds which are *poisonous* compared with the original bases. Curare itself contains the tertiary base Curine which is not very poisonous, as well as the far more poisonous Ammonium base Curarine. *Curine on methylation yields Curarine which is 226 times as poisonous as the original substance.*

The fact that the action of **Inorganic Salts** injected into the blood depends on the *electro-positive* half is analogous with the action of most **Esters** which generally resembles that of the **Alcohol** concerned—in both cases the **Acids** are usually physiologically inert.

Isomorphous Substances in a group have similar action, *e.g.*, **Li**, **Na**, **Rb**, **Cs**, **Ag**, **Tl**, and the physiological intensity usually increases proportionally to the **Atomic Weight**. **Potassium** and **Ammonium** are exceptions. In **negative elements**, *e.g.*, the **halogens**, there is no relation between physiological effect and atomic weights.

The toxicity of an element belonging to the same periodic family increases with increase in atomic weight—subject to variations. Some observations on the mechanism of Drug Action.—O.C.M. Davis, B.M.J. ii./22,11.

Ionisation plays an important part in the action of substances, *cf.*, HgCl_2 , which is ionised in solution and extremely poisonous and $\text{Hg}(\text{CN})_2$, which is almost non ionised (though soluble) and far less poisonous, *cf.*, also HgCl_2 and HgCl .

Meyer and Overton found that practically all narcotics are more soluble in **lecithin** and **cholesterine** than in water and they conclude that the narcotic value of a drug depends principally on its solubility in the liquid substances.—J. Grier, B. and C.D. i./13,282.

Schmiedeberg's Rules regarding action of **Aliphatic Compounds**.

The action of these depends on *volatility and solubility*, *cf.*, the lower with the higher members of the series of **Paraffins**.

(1). Poisonous radicles on substitution by simple **Alkyl groups** lose in intensity, *e.g.*, **Arsenious Oxide**, $\text{O}=\text{As}-\text{O}-\text{As}=\text{O}$ and **Cacodyl Oxide**, $(\text{CH}_3)_2\text{As}-\text{O}-\text{As}(\text{CH}_3)_2$.

(2). The effect of the **Alkyl groups** can on the other hand be lost or lessened by combining with other atoms or groups, *e.g.*, the **Mono-Di- and Tri-methylamine** behave like **Ammonia** and have no narcotic action, but the first rule holds here also as these **Amines** are less toxic than **Ammonia**.

(3). The action of a body made by *uniting two groups by an Oxygen atom* depends on the two components each acting separately. Where the two groups are similar or equivalent alkyl groups, *e.g.*, in the **Simple and Compound Ethers** then the action of the whole is simple and the resulting body resembles in action the corresponding **Alcohol**. Analogous are the **Esters**, the acids of which yield neutral (**Sodium**) **Salts** without any specific physiological action. **Acetic Ester** and its homologues are therefore classed with the **Alcohols**. If the **Acid** however has a specific action of its own then this shows itself in the **Ester** and has a modifying effect on the action of the **Alkyl group**,—*e.g.*, **Amyl Nitrite**.

The **Hydrocarbons** of the **Methane series** are less active than the **Ethylene**, **Acetylene** or **Benzene Series**. In the **Methane Series** commencing with the lower members we have the *anaesthetic and narcotic action*—this decreasing with loss of volatility and solubility. In the **Ethylene series** there is also evidence of narcotic action, *e.g.*, **Amylene**. The **Benzene compounds** show *paralyzing action on motor nerves* and further action on the *brain and spinal cord*.

Effects of Alkyl Groups.—Methyl groups introduced in Ammonia produce Tri-methylamine which is free from convulsive effects, *cf.* also the effect of introducing Methyl groups into the Amino group in Aniline, but if the Hydrogen of the nucleus be replaced by Methyl groups there is an increase in the effects, *cf.* also the methylation of Xanthine (*antea*). Replacement of the Hydrogen of a Hydroxyl group often reduces activity, *cf.*, Catechol $C_6H_4(OH)_2$ (1 : 2), Guaiacol $C_6H_4OH.OCH_3$ and Veratrole $C_6H_4(OCH_3)_2$. Again *Ortho*-methoxybenzoic Acid $C_6H_4OCH_3.COOH$ and Anisic Acid $CH_3O.C_6H_4.COOH$ are less active than Salicylic Acid $C_6H_4OH.COOH$, but this is not invariably true—Resorcin $C_6H_4(OH)_2$ (1 : 3) is far less poisonous than Dimethyl-resorcin $C_6H_4(OCH_3)_2$ (1 : 3).

Ethyl groupings have a marked influence in causing action on the *central nervous system*, more so than Methyl groups. Another interesting difference between Ethyl and Methyl groups is seen in *p*-phenetol-carbamide $C_2H_5O.C_6H_4.NH.CO.NH_2$ (Dulcin) which is intensely sweet and the *Methyl analogue* which is *tasteless*.

Ethyl groups occur in the following hypnotics. Ethyl Alcohol, Amylene Hydrate, the Sulphonal group, Urethane, Hedonal, Veronal.

In Veronal Class the group $CR_2.CONH.CO$ is a "hypnophore." To manifest hypnotic action without undesirable after-effects the two 5-alkyl groups of the Pyrimidine ring should together contain between 4 and 8 Carbon atoms, at least one group must be of open chain form. The Benzyl group is undesirable, the Carbamide group may not be replaced by the Amidine group, and the molecular weight should not exceed about 250.—A. W. Cox, *Jl. Amer. Pharm. Assoc.*, '23, 12, 602, per J.C.S., A. 1./24, 668.

The most active hypnotics belong to the aliphatic series and contain a quaternary Carbon atom linked to alkyl groups. Methyl derivatives are inactive, and hypnotic effect appears to increase with replacement of Methyl by homologous radicals up to a solubility limit.—J.C.S., A. 1./24, 1101.

Note also the harsh action of Acetanilide is greatly modified by the introduction of the ethyl group as in phenacetin.

Effect of Phenyl Group,—no general rule.

Effect of Hydroxyl Group.—In *aliphatic bodies* the Hydroxyl group usually weakens action and it is roughly proportional to the number of OH groupings introduced, *cf.*, conversion of the narcotic Alcohols into Glycols, Glycerol, Mannitol, etc.

The effect is otherwise however in the case of the *aromatic bodies*—the OH usually *increases* effect,—*cf.*, the obvious case of Benzol and Phenol also Benzoic and Salicylic Acids. The OH very often performs the function of an anchoring group, *e.g.*, for esterification.

Primary Alcohols as a generalisation are less active than secondary and these again less active than the tertiary.

'Ladenburg's Rule' that all tropeines with a mydriatic action must contain a Hydroxyl group and a Benzene nucleus is incorrect, and in any case Ladenburg never enunciated it.—P.J. i./26, 261.

Effect of Halogen.—

In aliphatic bodies there is *increase in narcotic power*, but there is *also an increase in depressant action* on the heart and blood vessels. The narcotic power and toxicity of Chlorine compounds is well seen in the case of the Chlorhydrins,—narcotics and vasodilators derived from Glycerin which is inert, Tri-chlorhydrin being most active and the Mono-compound least. Note that in the case of

the Trichlor- and Monochloroacetic Acid the toxicity is reversed. Halogen introduced in the Benzene nucleus causes little alteration in properties. Organic Iodine Compounds differ from those of Chlorine and Bromine in having greater antiseptic and toxic properties and diminished hypnotic effects.

Although the entrance of halogens increases the narcotic action of a drug, the molecule acts as a whole, neither Chlorine nor Bromine being set free in the tissues. Examples: Chloral Hydrate, Trichlorbutyl Alcohol.—J. Grier, B. and C.D. i./13,282.

Effect of Nitro- and Nitroso- Groups.

Either of these whether replacing Hydrogen in the nucleus or in an Hydroxyl Group causes *increased toxicity*. The Aliphatic Nitrites are *vasodilators*, cf., Amyl Nitrite. All the Nitrites act in this way, the secondary and tertiary being stronger than the primary, probably owing to the fact that they are more readily hydrolysed to Alcohol and Nitrite. Nitroglycerin and Erythrol Nitrate,—Esters of Nitric Acid show similar action. In the *Aromatic Series* a Nitro Group entering also usually *increases toxicity*.

The effect of the sulphuric (SO_4) group is non-permeating whilst the acetic radicle is so, also the ammonium radicle; this explains why ammonium acetate is actively diuretic whereas ammonium sulphate is slightly cathartic.—J. Grier, *ibid*.

Effect of Basic Nitrogen Groups.—This can produce in either series important changes to which P. May makes various references. The introduction of *Alkyl groupings* into such bodies reduces toxicity and as before gives *hypnotic effect*, e.g., Carbamic Acid NH_2COOH (poisonous) gives Urethane (Ethyl Carbamate)—more stable and hypnotic. Hydrazine $\text{NH}_2\text{—NH}_2$ is far more toxic than NH_3 , but the Tetra- and Penta- Methylenediamines are non-toxic.

The entry of the Amino Group into the Benzene nucleus forms the groundwork of a large number of antipyretics and analgesics. Aniline like Ammonia produces convulsions, but like Benzene it also causes paralysis of muscles and nerves, and if one of the Hydrogen atoms of the NH_2 group be replaced by Alkyl the convulsions disappear but the paralysing action remains. If a Hydrogen atom in the nucleus be replaced by a single atom, e.g., Bromine, the convulsive effect is retained, and if it is replaced by an alkyl group the effect is increased, but if a complex group, especially an acid group, e.g., SO_3H , enters the nucleus, the effect is lost, e.g., in Amino-Benzene-Sulphonic Acid $\text{C}_6\text{H}_4\text{.NH}_2\text{.SO}_3\text{H}$. All these derivatives e.g., Aniline have a toxic action on the blood, forming Methæmoglobin. As a rule aromatic derivatives of NH_3 *lower temperature*.

Effect of the CN radicle.—Isocyanides (Isonitriles) cause paralysis of the respiratory centre and the Cyanides (Nitriles) produce coma. Neither, however, are as poisonous as HCN. The lower members in the fatty series, CH_3CN and $\text{C}_2\text{H}_5\text{CN}$ are less poisonous than the higher—Cyanacetic Acid CNCH_2COOH is practically non-toxic. Cyanogen Chloride CNCl on the other hand is very toxic as it yields readily HCN.

Effect of Aldehyde Groups.—

Formaldehyde is very reactive chemically and physiologically. It is a strong irritant on the mucous membrane. Acetaldehyde produces excitation, and then anaesthesia. Paraldehyde is stronger in action than the latter. *By entry of OH into the Aldehyde molecule and by condensation of these bodies to form Aldols, reactivity is lowered*, as also physiological power,—the sugars are practically inert. The aromatic Aldehydes are of low toxicity.

Effect of Ketones—Similar to Alcohols,—narcotic. Hypnotic action is seen in the Mixed Ketones, *e.g.*, Acetophenone $C_6H_5.CO.CH_3$.

Effect of Acid Groups. These cause generally a *decrease in activity* or total suppression, *e.g.*, substances containing an OH group on combining with *Sulphuric Acid* lose their toxicity—Phenol is toxic but Phenyl Sulphuric Acid is harmless, *cf.*, also Morphine $C_{17}H_{17}NO(OH)_2$ —Morphine- Sulphuric Acid $C_{17}H_{17}NO(OH).O.SO_2.OH$ —this latter, as already referred to, is practically inert. The Sulphonic Acids of various drugs are in nearly every case of little use, the introduction of *Carboxyl* (COOH) is almost analogous. COOH for example reduces toxicity of Benzol which can be taken in doses of 8 Gm. per day to 12 to 16 Gm. of Benzoic Acid. Methylamine NH_2CH_3 is toxic. $NH_2CH_2.COOH$ (Glycine) is harmless. The *mere addition of Acid radicles* without converting the body into an Acid may suffice, *cf.*, NH_3 poisonous, NH_2CO-CH_3 Acetamide practically harmless. Acetanilide is less poisonous than Aniline. The addition of Acid radicles to active bases is useful in synthesis of drugs,—especially with regard to **Acetylation of the NH_2 Group**,—to weaken basicity and *retard action*. Acetyl, Lactyl, Benzoyl and Salicyl are used, but the *Acetyl* has advantages over the others.

Practically all *synthetic antipyretic* and *analgesic* drugs contain the *acetyl radicle*. Not only so but it occurs in such naturally occurring pain-relieving drug-principles as aconitine and colchicine.—Grier.

Unsaturated Links. Unsaturated substances are usually more toxic than the saturated. Allyl Alcohol $CH_2=CH.CH_2.OH$ is strongly poisonous, but is not narcotic. Propyl Alcohol $CH_3CH_2CH_2.OH$ is narcotic, but not really poisonous. This relative toxic action is a general property of unsaturated as compared with the corresponding saturated bodies.

Molecular Weight, Isomerism, etc.—

Increase in Molecular Weight in homologous series generally produces *increased toxicity*. Several instances in which *stereoisomerides* differ are given, *e.g.*, Isopilocarpine and Pilocarpine, Maleic and Fumaric Acids, Atropine and Laevo Hyoscyamine, Dextro and Laevo-Nicotine and the natural Adrenalin which is about 11 to 12 times as active as the Dextro compound. With regard to *ortho*-, *meta*- and *para*- Benzene derivatives, no generalisations can be made. *Para*- compounds are often more poisonous than the *ortho*. (In this connection it is interesting to note that the *para* analogue of saccharin is tasteless.)

With regard to **changes that take place on the passing of an organic drug through the system**, already referred to, the following is of interest,—*Salts of Organic Acids are generally decomposed into the free acid and a Chloride of the base*, but *Esters* and similar bodies are in the majority of cases *undecomposed* by the *gastric contents*. In the small intestine, however, the drug encounters the pancreatic enzyme trypsin and an alkaline medium. Trypsin has marked hydrolyzing action on Esters, Anilides and similar bodies,—*here after saponification the components of the drug exert their specific action*.—The generally accepted decomposition of Acetyl-Salicylic Acid in the intestine is here pointed out, to which we have devoted some attention, *vide Vol. I.*, p. 75, and *this Vol.*, p. 15.

Aliphatic bodies suffer usually complete oxidation to Carbon Dioxide, Water and Urea. Aromatic bodies on the other hand maintain the nucleus, the decomposition being concentrated on the side chains.

From "The Chemistry of Synthetic Drugs," by Percy May, D.Sc. (Longmans, Green and Co., 1921). By permission of the author.

Brunton and Cash pointed out that all open chain substances, the types of which are Marsh Gas and Chloroform, paralyse the nerve centres and tend to anæsthetic action, whilst the ring series produce convulsions or spasms before paralyzing.

Binz, of Bonn, experimenting in 1867 (prior to Ehrlich) on the action of various drugs on the infusorial organisms found that active paramecia were readily destroyed by a 1 in 10,000 solution of Quinine, though they withstood enormously stronger solutions of Strychnine and other poisonous vegetable substances. This led to the conclusion (the cause of malaria being unknown at the time) that malaria would be found to be of protozoan nature since malaria was so readily cured by Quinine and, secondly, that in giving 15 grains of the Hydrochloride to an average man a solution of twice the strength in the blood necessary to kill amœbæ would be formed, thus fulfilling the *therapia sterilisans magna* idea of Ehrlich.

Pharmacological Action in relation to Chemical Constitution.—C. R. Marshall, P.J. i./13,622. We refer to this paper elsewhere, *e.g.*, under Nitroglycerin *Vol. I.* See also J. M. Fortescue-Brickdale, B.M.J. i./15,106; F. L. Pyman, L. ii./17,924.

Relation between Chemical Constitution, Chemotherapeutic Action and Toxicity—E. L. Walker and M. A. Sweeney, Jl. Ph. & Exp. Ther., June, '27, 87.

Arsenical Drugs with quinquevalent Arsenic, Atoxyl, Tryparsamide, etc., frequently affect the optic tract, while trivalent compounds, such as Arsenobenzol, do not. It was found by experiment however that the valency of the Arsenic is not the most important factor, optic lesions being produced by compounds containing an amino group in the para-position to the Arsenic, but not in the ortho- or meta- position.—A. G. Young and A. S. Loevenhart, Jl. Pharm. Exp. Ther., '24, 23, 107, per J.C.S., A.i./24,689.

STERILISATION.

Apparatus.—For the bacteriological sterilisation of apparatus—bottles, mortars, measures, pipettes, ampoules, etc., before filling, chemical cleanliness is first necessary. Use soap and hot water, rinsing with tap water, then 'burning off' with a little Sulphuric Acid, rinsing again and drying. A solution of Potassium Bichromate in Sulphuric Acid 46 and water 30 is useful. The apparatus is then to be heated in a hot (dry) air oven at 150° C. for three hours or at 170° C. for one hour.

An oven, provided with a thermometer, may be improvised. A shelf or false bottom perforated or so arranged for air circulation

must separate the articles from the bottom plate, whereon the flame plays. If it be desired to prepare a supply of utensils in this manner, it is convenient to wrap in stout filter paper, cotton wool or lint, *before* placing in the oven, this wrapping remaining on until the Apparatus in question is required for use. In place of the hot air oven a steam steriliser or Autoclave (a steriliser by steam under increased pressure) may be used, as described under 'Liquids,' but on the whole dry heat is best.

Ampoules, etc., for Alkaloidal Salts Solutions should first be washed with Dilute Hydrochloric Acid to remove superficial alkali, and then with clean water before sterilising.

Ph. Ital., orders glass ampoules and bottles for hypodermic injections to be tested for alkalinity:—Ten to twelve ampoules or five to six bottles are filled with a clear solution of 1% Mercuric Chloride, and sealed. After $\frac{1}{2}$ hour in an autoclave at 112° C. no brownish turbidity should be perceptible.

Dry Chemicals.—For these dry heat is best—it should, if possible, be as high as 150° C. and be continued for at least half an hour,—subject, of course, to the physical characters of the substance permitting it (decomposition, M.Pt., volatilisation, loss of water of crystallisation, etc.); or the sterilisation may be done in the autoclave at 115 to 120° C. for fifteen minutes, but owing to solubility in the steam many dry substances cannot be so treated—for **Liquids** however, the Autoclave has many advantages, *v. infra*.

It is convenient in sterilising a bottle full of dry medicament, for example, **Boric Acid Crystals** or a **Zinc Oxide Dusting Powder**, to plug the neck of the bottle with a fairly tight wad of cotton wool (preferably previously sterilised to scorching point in the hot air oven). A supply of this wool should find a place in the Dispensary *kept in a glass jar with closely fitting lid*. The stopper of the bottle is treated separately,—it may be laid alongside the bottle in the oven at the time of heating (ordinary corks are bacteriologically unsuitable). After heating, the bottle and contents are first allowed to cool down gradually—preferably *in the oven* before stoppering,—this ensures that the stopper will not 'jam.'

It is a good plan to grease the ground surface of the stopper with a minute layer of Soft Paraffin,—this is done *after sterilising* and *just before inserting into the bottle* (which is effected simultaneously with the removal of the wool plug) by passing it 2 or 3 times through the Bunsen flame. The whole procedure is carried out dexterously to prevent access of air organisms. (Note, that bacteriologists would burn the exuding portion of the cotton wool plug and quickly blow it out, leaving sufficient to catch hold of—simultaneously allowing the flame to play on the neck of the bottle also).

For sterilisation by dry heat, three hours at 150° C. is adequate or one hour at 170° C. (this latter treatment is sufficient to kill all the usual polluting organisms.)—Muir and Ritchie.—We have modified the time requirement somewhat in respect of Dry Chemicals.

Tawell advises sterilising powdered boric acid by prolonged heating at 98° C., in a carefully regulated air-oven to give satisfactory results. It is liable to undergo change if much heated above 100° C.

Liquids :—

The boiling of a liquid for five minutes is sufficient to kill ordinary germs if no spores are present. The boiling of any fluid at 100° C. for $1\frac{1}{2}$ hours will ensure sterilisation in almost any circumstances.

To ensure the killing of spores it is customary to heat liquids where spore contamination is likely (spores of the *Tetanus Bacillus*, *Anthrax Bacillus*, and the ubiquitous *B. Subtilis*, the Hay organism) in an ordinary steamer on three successive days ($\frac{1}{2}$ to 1 hour). By this treatment all bacilli present are killed on the first day; spores present may develop and are killed on the second day, and the third day is to ensure absolute sterilisation,—this is a modified ‘Tyndall’s Intermittent Sterilisation.’

The Spores of the Hay *Bacillus* are not killed by boiling for about ten minutes (M. and R.).

Some flint bottles (even ‘Winchesters’) will stand heating in the autoclave. A stoppered bottle should be used.

The subsequent ‘stoppering’ of a bottle of this kind is conducted as described under ‘Dry Chemicals.’ Working on these lines it is quite easy to bottle off liquids (e.g., Broth used in bacteriological work) in such a way as to keep good for years,—indeed indefinitely. Rubber corks are also applicable,—these must be boiled before use.

It is an advantage to heat Solutions in a suitable **Steam Steriliser**, for under pressure practically no evaporation takes place from the Solution, as it is surrounded by an atmosphere saturated with water vapour (quite apart from this, steam sterilisation in general is more efficacious than dry heat). The temperature employed in an autoclave is usually 115 or 120° C. To boil at 115° C. water requires a pressure of about 23 lbs. to the square inch (i.e., 8 lbs. + the 15 lbs. of ordinary atmosphere pressure). To boil at 120° C. a pressure of about 30 lbs. (i.e., 15 lbs. + the usual pressure) is necessary. These pressures would usually be called 8 lbs. or $\frac{1}{2}$ atmosphere and 15 lbs. or 1 atmosphere respectively. In an autoclave of this kind the desired temperature is maintained by adjusting the safety valve so as to blow off at the corresponding pressure.

Cautions:—In all cases it is necessary to allow the Autoclave to cool well below 100° C. before opening, otherwise there will be a sudden development of steam when pressure is removed and fluid will be blown out of the vessels under treatment. Some Autoclaves are not fitted with a thermometer,—in this case expel all air contained initially, otherwise a mixture of air and steam being present the pressure read off the gauge cannot be accepted as an indication of the temperature. Furthermore care must be taken to ensure the presence of a residuum of water when steam is fully up, otherwise the steam is superheated and the pressure on the gauge again does not indicate the temperature correctly.—M. and R.

A single exposure of 15 minutes in an Autoclave is sufficient to destroy all bacilli and spores, provided the steam pressure is at least two atmospheres, i.e., temp. 120° C. approx. or 15 lbs. pressure on the gauge.

Low temperature sterilisation:—Few ordinary organisms in a spore-free condition will survive a temperature of 57° C. if long enough applied; hence Solutions or preparations which will not stand boiling can be rendered practically sterile by heating in a water bath on three successive days at about this temperature—60° to 70° C. is commonly used. The object here is to kill off spores on the same lines as before and such procedure will obviously kill off the non-spore-bearing pathogenic bacteria.

We have found 10 days intermittent heating in this way insufficient to kill *B. subtilis* spores.

*Special Remarks.***Hypodermic Injections and other Solutions of Organic Compounds :—**

Suspensions or Emulsions of Chemical Substances decomposed by heat, *e.g.*, Emulsion Iodoformi, may be prepared by *first sterilising the suspending medium, cooling and then preparing the suspension in a sterilised moriar*,—the same remark applies to Hypodermic injections of decomposable substances in 'Vegetable Oils.' The Ph. Ital. directs that ordinary Hypodermic Solutions are to be sterilised at 160° C. for 30 minutes or by heating in an autoclave.

According to this Pharmacopœia—Solutions of substances which are decomposed by a temperature of more than 100° C.—viz., Cocaine Hydrochloride, Morphine Hydrochloride, Atropine Salts, Quinine, Eserine Sulphate, Strychnine, Adrenalin, Cacodylates, and Stovain—are to be prepared with Sterile Water and the container then placed in a water-bath for fifteen to twenty minutes, so that the level of the boiling water in the bath corresponds to that of the solution in the bottle. Solutions of *substances decomposed at about 100° C.* are exposed to a temperature of 58° to 60° C. for one hour daily on four consecutive days. This applies to Serums, Organo-Therapeutic Preparations, Ergotin, and Glycerophosphates. Oily Suspensions of Calomel, Yellow Oxide of Mercury, Lecithin, and Camphor are to be prepared with sterile materials, then placed in a boiling water-bath for ten minutes or in an air-bath at 100° C.

Note.—We do not agree that all the first mentioned are decomposed as stated at a temperature of more than 100° C.—W. H. M.

Ophthalmic Solutions.—

Remarks under Apparatus and Hypodermic Injections apply here. In dispensing simple Ophthalmic Solutions required for immediate use, *e.g.*, Atropine, Cocaine, etc., Solutions, in Chalk's Dropping Bottles it will be only practicable to thoroughly steam the measure, bottle, rod, etc., and prepare the Solution by dropping the Alkaloidal Salt into the bulk of the required amount of hot water or other diluent—making up to volume on cooling. *Note.*—Cocaine, Atropine and Eserine Salts are *not* decomposed by this procedure. *Sterilised bottles wrapped in Filter paper should be kept ready in the Dispensary.*

Ointments may be sterilised by shaking melted ingredients in a closed tin until cold. In the case of Ointments containing ingredients decomposed by heat it will be necessary to sterilise the non-decomposable items, and to incorporate in a sterile mortar with the decomposable items. In some cases the latter may be sterilised by shaking with Alcohol and subsequently with Ether if insoluble in these two liquids.

Surgical Instruments.—In boiling these (knives, forceps, etc.) Sodium Carbonate solution 1% is used or air-free (boiled) distilled water to prevent rust.—W. K. Fitch.

A mixture of Liquid Paraffin 2, Chloroform 16, and Alcohol 95% (containing Liq. Cresol. Saponat. 2%) 16, found best.—M. H. Post, Am. Jl. Ophthalm.

Lysol 15 minims, Ether 2 drachms, Industrial Spirit to 1 ounce, suggested for keeping sterile syringes and needles.—F. F. Ward, B.M.J. ii./27, 1214.

The use of Mercury compounds on Instruments.—Experiments in our laboratories (1925) showed that immersion for many hours in **Ether Soap with Mercuric Iodide** or in a 1—50 solution of **Mercurochrome** had no visible effect on the instruments. **Mercury Potassium Iodide** (1—2,000) and **Mercury Oxycyanide** (1—1,000) solutions stain the metal after a short time, while **Mercury Oxycyanide** (1—200) and **Mercuric Chloride** (1—1,000) have almost an immediate action.

Mercury Biniiodide for disinfection is unjustified. Steam-washed catgut ribbons immersed in a 1 in 1,000 solution of Mercuric Iodide for 1,710 days were still infected at the end of that time.—H. Candy and W. Bulloch, L. ii./28, 769. *This certainly seems to need further investigations, we are at a loss to understand the statement.*

Surgical Dressings :—

For sterilising Surgical Dressings, the dressings are wrapped in cotton wool or in cloths or towels and sterilised by superheated steam; for convenience they may be packed in tins. The air is then exhausted at 20 ins. pressure; steam at $260^{\circ}\text{F.} = 126.6^{\circ}\text{C.}$ is introduced, and is forced through the dressings for 20 minutes. They are finally exhausted by reduced pressure (vacuum of 20 ins.) for 20 minutes and on removal rapidly soldered down. 'Dressings Boxes' are also used with holes in the sides which allow of passage of steam through the dressings—which are closed instantly on removal—soldering is preferable.

Failing superheated steam a current of steam for $1\frac{1}{2}$ hours may be used.

The **Vacuum producing** arrangement in the sterilisers ensures the subsequent thorough penetration of steam into the interior of the dressings and on completion of the sterilising the steam is removed by the re-exhaustion. The Apparatus is provided with an **air filter** to contain cotton wool or other medium, through which the air is drawn into the chamber at the close of the operation.

The heating of sterilisers of this description is done either from an existing or separate steam boiler, or by gas or oil burners, or by combination supply alternately, *e.g.*, steam and gas, oil and gas, oil and steam, as occasion requires. In this way, except in the first case, the steriliser may, if desired, be worked by steam from an absolutely pure source, *e.g.*, sterilised distilled water.

For testing the efficiency of sterilisation, the following are used :—

Acetanilide and Methylene Blue Tubes. *Syn.* TUBES TÉMOINS.

Sealed glass tubes filled with Acetanilide Powder and containing in addition in the centre a small pinch of Blue Dye. These are placed in sterilisers to determine whether sterilisation has been adequate and has penetrated into the centre of the dressings. Acetanilide melts at 113°C. , hence if this temperature has been reached the contents of the tube on removal should be evenly blue throughout.

Malic Acid is used also for similar purposes. This melts at practically 100°C.

Powdered Sulphur an ideal pyrometer for testing sterilising of dressings inside drum. M.pt. 114.5°C. and is unaffected by moisture. Sulphur should be in a small packet introduced into middle of dressings, a piece of black thread tied to centre of packet and leading to top of dressings enabling it to be withdrawn.—H. Halliday, I.M.G., Oct., '25, 457.

Phipson's Temperature Indicator consists of a simple electric bell circuit, with the bell, a small dry battery and switch outside and the two leads passing into the steriliser and terminating in a small heat-operated control. The control consists of fusible alloy permitting a plunger (passing through a spring) to complete electric circuit. Alloys melt at 83, 99 and 113°C. —made by Johnson, Matthey & Co. The indicator by C. F. Casella & Co., Parliament Street, London.—Maj. E. S. Phipson.

Metal alloys (Albert Browne, Ltd., Chancery St., Ldn.), fusing at given temperatures, used for the purpose, also sealed tubes of a standard solution of Glucose and Sulphuric Acid—colour changes slowly at 212°F. , but at 239°F. they show coloured to black according to time.—R. J. B. Hall and A. W. Chapman, B.M.J. i./25, 1119.

Rubber Gloves Sterilisation.

The process employed in hospitals is to sterilise at 230°F. for 20 minutes. We had occasion (1927) to test a British-made glove, the "**Veedip**," and two well-known American makes, by heating at that temperature on successive days. After 10 treatments the American gloves failed to pass a rather severe stretching test, while the English gloves were practically unaffected by the heating.

Sodium Bicarbonate.—To sterilise a 5% solution (much used in place of normal saline) it is best to steam in a Koch steriliser. Boiling at ordinary atmospheric pressure causes some decomposition.—E. J. Hart, P.J. i./19, 59.

Quinine Acid Hydrochloride may be sterilised at 115°C. in an autoclave for 15 to 20 minutes.

A list of temperatures suitable for a variety of chemicals is given.—P.J. i./19, 34.

ANTISEPTIC POWER OF NUMEROUS CHEMICALS AND DISINFECTANT PREPARATIONS.

There seems to be almost a deliberate conspiracy in this country to discredit disinfectants, as useful weapons with which to fight the germs of disease. Any agent may be puffed up as a disinfectant and false claims made for its powers, and the sale of relatively poor and inefficient agents is fostered by the conditions imposed upon the sale of disinfectants, as *under the Poisons & Pharmacy Act of 1908 comparatively useless agents containing not more than 3% of Carbolic Acid or its homologues need not be labelled 'Poisonous'*, and can be sold at oil and grocery shops. Therefore the Act tends to favour the sale of low-class disinfectants, for the public buy far more disinfecting material from oil and grocery shops than from chemists. Perhaps the nature of the germicidal action of disinfectants is, in order of importance, (1) chemical; (2) physical; and (3) electrical.—H. R. Kenwood, L. i./26,1056.

Of the various methods of assaying the value of a disinfectant the Rideal-Walker method gives satisfactory valuation.

RIDEAL-WALKER TEST.

The following is a brief description of the improved technique (1921) of this test.

MATERIALS REQUIRED FOR TEST.

Nutrient Broth. This is prepared by boiling a solution of Peptone 20 Gm., Liebig's Extract of Meat 20 Gm., Sodium Chloride 10 Gm., in one litre of Distilled Water for 30 minutes, filtering, neutralising to Phenolphthalein, and then adding 15 Cc. N.Hydrochloric Acid. After sterilising, broth tubes containing 5 Cc. are prepared.

Standard Carbolic Acid. Phenol of commerce is liable to be contaminated with small quantities of Cresols, which render it unreliable for bactericidal control, the impurity being detected by a lowering of the solidifying point. After melting 50 Cc., the Standard Carbolic Acid should solidify at above 40° C.

The CRESOLS as impurity are not easily shown by a Koppeschaar determination but are detected by estimation of the Solidifying Point.—J. T. Ainslie Walker and J. M. Weiss, 'Medical Officer,' 12 May, 1923.

The Culture. *B. typhosus*, grown in the above broth, and incubated for 24 hours at 37° C., is employed.

TECHNIQUE.

A test is first carried out with 5 dilutions of the Standard Carbolic Acid, in order to ascertain the strength (usually about 1 in 100) which allows the organism to survive after 2½ and 5 minutes contact, but kills in 7½ minutes.

Four suitable dilutions of the disinfectant under examination are then prepared with sterile Distilled Water, e.g. 1 in 1,900 1 in 2,000, 1 in 2,100, 1 in 2,200, for a disinfectant having a coefficient of about 20. 5 Cc. of each of these solutions and 5 Cc. of the Carbolic Acid control are taken in test-tubes, and at intervals of 30 seconds, 0.5 Cc. of the culture are added by means of a pipette. When 2½ minutes have elapsed since culture was added, a broth tube is inoculated from each solution, using one loopful of a standard Platinum loop (4 mm. internal diameter). Broth tubes are similarly inoculated after 5, 7½ and 10 minutes contact, and are then all incubated at 37° C. After 48 hours, the tubes are examined and the strength of disinfectant (e.g. 1 in 2,100 is) noted, which, like the Carbolic Acid control, permits growth after 2½ and 5 minutes, but kills in 7½ and 10 minutes.

Then the *Rideal-Walker Coefficient* is

$$\frac{\text{dilution of disinfectant}}{\text{dilution of Phenol control}} \quad (\text{i.e., for the example given, } \frac{2100}{100} = 21)$$

The Rideal-Walker method has been largely used by the War Office.

The figure for a disinfectant varies for different organisms.

We have for some years been engaged in practically determining the antiseptic powers of general chemicals and proprietary disinfectants.

Our early work (started in 1908) was conducted with a *variety* of organisms (*B. Typhosus*, *Staphylococcus*, *B. Anthracis*, etc.), but it is obvious that only by using what may be termed a Standard Type of Organism, e.g., *B. Coli*, and using identical conditions, can comparative results be arrived at. As the earlier work was done with this organism we continue to make use of it. In some cases notes on results with other organisms are added or retained where of interest.

We have found that some substances, e.g., *Saccharin Insoluble*, acts as a germicide on *B. Coli* but not as a fungicide.

The suggestion has been made to alter the Rideal-Walker Coefficient Method of examining Disinfectants by introducing organic matter—milk, urine, fæces, etc.—into the disinfectants, as it is claimed that the real test of a disinfectant is the strength and time of exposure which will enable it to kill organisms in the presence of such, but the idea has met with disfavour; and here again we fail to see how any uniform simple standardisation can be introduced with the interference of such substances.

The importance of distinguishing the mere inhibitory or antiseptic action from the germicidal power has been emphasised. Experiments showed that the first product of action of Mercuric Chloride on bacteria (? Albuminate of Mercury) remains when sufficiently diluted in such a way as to prevent growth, but when the Mercury is removed, as by Ammonium Sulphide, the bacteria resume activity. Hence in all testing of disinfectants the actual death of the organisms should be ensured.

Reports on disinfectants which combine with protein or other matter or which oxidise it, must be regarded with caution when investigations have been conducted on bacteria in the absence of such organic matter (Phenols and Phenoloids are little affected by organic material of this kind). It is important to realise that the action of disinfectants is affected by proteins, fats, urea, uric acid, organic and inorganic salts, alkalis, acids, masses of non-pathogenic bacteria, cells, etc.

Emery's Method.—Citrate Blood used as diluent with *S. faecalis* as organism. It is shown that Carbolic Acid is about 70 times as strong as Eusol and Dakin's Solution. Malachite Green is the most potent of the antiseptics examined.—W. D'Este Emery, L.i./16,817.

In the interests of humanity and honest trading, it is clearly essential that official control should be exercised over proprietary antiseptics, and that their potency should be stated on the labels according to an official standard method.—W. H. M., Medical Press. cf. S. Rideal, L. ii./13,826.

The "Lancet" Carbolic Acid Coefficient. The figure representing the percentage strength of the weakest lethal dilution of the Carbolic Acid control, using *B. Coli* as test organism, was divided by

the figure representing the percentage strength of the weakest lethal dilution of the disinfectant being tested. This was done at $2\frac{1}{2}$ and at 30 minutes and a mean of the resulting figures was taken as the *Carbolic Acid Coefficient*.

The Bacteriological and Chemical results included the following :—

COAL TAR DISINFECTANTS FORMING EMULSIONS WITH WATER.—					
	Co- effi- cients.	Phenols or Pheno- loids.		Co- effi- cients.	Phenols or Pheno- loids.
Cofectant ..	9·8	66·27	Pearson's Anti-		
Sanitas Bactox	9·5	39·7	septic Fluid.	2·2	20·7
			Jeyes'		
Cyllin ('bulk')	8·8	40·41	(Chemists')	1·7	17·8
			Zotal	1·5	10·0
Kerol	7·7	40·56			
Izal	7·4	41·35	Jeyes' No. 2		
			(Grocer's) ..	0·75	5·13
Cyllin Medical	6·4	32·08			

CLEAR WITH WATER.—

	Co- efficients.	Phenols or Phenoloids.		Co- efficients.	Phenols or Phenoloids.
Crude Carbolic			Calvert's No. 5		
Acid.. ..	4·2	82·65	Carbolic Acid	2·5	93·26
Trikresol ..	2·5	—	Lysol	1·7	50·96

It should be noted however that the figures for Phenols or Phenoloids were obtained by simple extraction with a solvent, the Phenol content indicated by *Bromine—the more scientific method*—was considerably less (about $\frac{1}{2}$ in many cases).

Modification of the "Lancet" Method. A 24 hour culture of *B. Coli* is used ; the experiments are carried out at 20° C. ; the proportion of culture to disinfectant is 0·1 Cc. of culture to 5 Cc. of disinfectant ; the amount of inoculation into subculture tubes is measured by loops ; the medium for subculture is prepared from beef extract according to the American standard and has a reaction of +1·5, the titration being carried to a point where the pink colour is distinctly perceptible.—*Jl. Infectious Diseases*, Jan., 1911, per leader in "Lancet," i./11, 43.

Experiments to determine how rapidly antiseptics pass through animal membrane as estimated by destruction of bacteria. The membranes employed were celloidin and the omentum, mesentery, diaphragm and skin of the rabbit. Carbolic Acid and Mercuric Chloride were without action in 24 hours. There was, however, one exception, *i.e.*, a 5% Aqueous Phenol Solution was found to pass through the diaphragm of a rabbit in five minutes.

The most effective proved to be Iodine and Alcohol.—*L. i./11, 1366*.

The Edmunds' Cell method using Agar Slabs to determine the diffusibility of antiseptics is referred to, Vol. I., p. 36. Edmunds and his co-workers found Iodine in such circumstances a poorly diffusible bactericide.

Mechanism of Disinfection.

Formaldehyde, Halogens, Mercuric Chloride, Acids and Alkalis form chemical combinations with Proteins. The action of Phenols and Cresols in regard to Proteins is not understood. Alcohol depreciates whilst Hydrochloric Acid increases effect of Phenol. Meta-cresol precipitates Proteins in lower concentration than Phenol hence it is more active. E. A. Cooper evolved a theory

that the action of Phenols on bacterial proteins is not directly bactericidal. The germicidal action which follows absorption does not seem to be the result of a typical chemical union between the Phenols and bacterial Proteins.

E. K. Rideal puts forward a theory of the Mode of Action of Disinfectants on modern physico-chemical views.—B.M.J. ii./23,1271.

Specificity in Antiseptics.

Specific antiseptic treatment of infected wounds has been suggested.

Data are given *re* inorganic and organic acids operating on growths of *Streptococcus Pyogenes*, *Staphylococcus Aureus*, *B. Pyocyaneus* and *B. Aerogenes Capsulatus*. There is no great divergence either in strength or in point of the organisms in case of the inorganic acids (Hydrochloric and Nitric Acid) tested, but *re* the organic acids there are points of interest, *e.g.* Tartaric and Malic Acids are active on *B. Aerogenes*, whilst relatively non-active on the cocci. Malic Acid is further fairly active against *B. Pyocyaneus* and most active of all against the gas bacillus.

With regard to generally recognised antiseptics, Phenol and Cresol are more active against *Streptococcus* than against *Staphylococcus*, and showed very little activity against the gas bacillus. Quinine Hydrochloride showed its greatest activity against the gas bacillus, was fairly active against *Streptococcus*, but little on *Staphylococcus* and less still on *B. Pyocyaneus*. Sodium Fluoride is less active against the cocci and *B. Pyocyaneus*, but active against the gas organism. The best against the gas organism of all the bodies tried seem to be Salicylic Acid and Quinine Hydrochloride.

Clinically the values of Acetic Acid Dressings 1% in *B. Pyocyaneus* cases; of Sodium Bicarbonate 1% in *Streptococcus* cases; of Cresol 0.1% and Dakin's Solution in *Staphylococcus* cases and of Quinine Hydrochloride 0.5% in gas bacillus cases, especially the latter—are proven. Quinine seems to be the only specific against this organism. Further study may discover dressings specific for one or more groups of bacteria.—K. Taylor, L. i./17,294,306.

Selective bactericidal action. The chemical germicides, those that react with constituents of protoplasm, have a more powerful action on *B. coli* than on *B. pyocyaneus*. Formaldehyde is an exception, attacking both equally. Germicides which exert a physico-chemical action, such as aliphatic Alcohols, Phenols, *etc.*, are more active towards *B. pyocyaneus* than *B. coli*, and their action resembles that of heat.—E. A. Cooper and G. E. Forstner, Biochem J., '24,18,941, per J.C.S., A. i./24,1386.

Pasteur and his work—an interesting historical survey of science and medicine.—Louis W. Sambon, Jl. Trop. Med., May 15/23,153.

Coal Tar Dyes as Antiseptics.

Fairbrother and Renshaw adopt a grouping of the Coal Tar Dyes on the basis of the configuration of their molecules thus: (1) the azo class, (2) the triphenylmethane class, (3) the phthaleins or pyronones, (4) the azines, (5) the acridines, (6) the sulphur dyes, (7) the oxy-ketone dyes, (8) dyes of the indigo class. The last three being insoluble in water are unsuitable as antiseptics. Generally, dyes with marked antiseptic action on bacteria or protozoa contain one or more amino groups in the molecule. While presence of amino groups is not enough to cause antiseptic action, such action is not obtainable in their absence.—T. Stephenson, Pres., June 24/239. See also Auramine *postea*.

Comparative Value of Skin Antiseptics.

Acriflavine 5% in 50% Alcohol proved most efficient; then Acriviolet 2% in 50% Alcohol; then 5% Alcoholic Iodine; then Acriviolet 10% aqueous and Harrington's Solution, Picric Acid 5% in 95% Alcohol and Mercurochrome 5% in 50% Alcohol being least effective.—M. B. Tinker, Ann. Surg., Oct., '25, per Jl.A.M.A., ii./25,1668.

Study of 1,550 cultures showed that Iodine, Trinitrophenol, Harrington's Mercuric Chloride Solution, Mercurochrome, and Potassium Mercuric Iodide, will not kill most of the resistant, and some of the less resistant, pathogenic bacteria under conditions of perfect contact, and are still less efficient if penetration is required **Acriflavine 5% in 50% Alcohol** and 10% Acetone the most efficient antiseptic. Aniline dyes deserve further investigation.—M. B. Tinker and H. B. Sutton, Jl.A.M.A. ii./26,1350. See also *ibid* 1/27,1560.

We do not agree with the findings in the last two papers, but insert them as relevant. Acriflavine is NOT a potent antiseptic as ordinarily understood.—W.H.M.

The Phenol Coefficient is dependent on the **Hydrogen Ion Concentration** at which the broths are filtered during standardisation process, a broth with pH 7.6 giving results comparable with accepted R.W. values.—per C.D., i./27,373.

A modified U.S. Hygienic Laboratory Method for the coefficient using *Staphylococcus aureus*.—Y.B.P., '27,350.

So far it will be seen we have mainly dealt with various Proprietary (mostly Cresylic) Disinfectants. In 1914 we commenced to operate on a number of recognised antiseptic bodies and other substances not hitherto examined, and have incorporated our results in the following pages.

Somewhat curiously amongst the *relatively potent* are Thorium Nitrate, Acetic Acid, Acid Citric, Acid Lactic, Acid Picric, Alcohol 70%, Potassium Chlorate, whilst on the other hand the *impotency* to kill disease organisms of the following chemicals—Antimony Potassium Tartrate, Arsenious and Arsenic Oxide, Arsamin, and Acetone—is of interest.

All the results have been obtained by procedure strictly in accordance with the "Lancet" Method. For practical purposes an exact determination of the Coefficient is not necessary. *All that the practitioner wants to know is, whether a specific disinfectant will kill the organism in a reasonable time—if in the prescribed 2½ minutes so much the better*—this we have stated, also in many cases a figure for the result of 30 minutes contact.

A good disinfectant must have high germicidal power, must not be affected markedly by heat, should have no corrosive action on metals; is must be miscible or form a fine emulsion and with water.

Prof. Hewlett some years ago made the useful suggestion to employ a **Torch Flame** generated by a cyclone burner burning paraffin, similar to that used on night works, &c., **for disinfecting walls, floors, &c.**

THE MOST POTENT ANTISEPTICS.

The following, according to our experiments, have practical value, i.e., they are germicidal (to B. Coli) in the strengths indicated in 2½ minutes under laboratory conditions.

Acetanilidum -	- 1 in 400	Acidum Salicylicum-	1 in 1,000
Acidum Benzoicum	1 in 500	„ Sulphuricum	1 in 200
„ Carbolicum*	1 in 80	Alcohol -	- 70%
„ Chromicum	1 in 40	Argenti Nitras	- 1 in 2,000
„ Cresylicum	1 in 200	Brilliant Green	- 1 in 100
„ Formicum		Bromum	- 1 in 200
„ (actual) -	1 in 20	Chlorinum	- 1 in 20,000
„ Hypochlorosum,		Chloroformum	1 in 75,000
see Eusol		Creosotum	- 1 in 300
„ Lacticum -	1 in 100	Dakin's Solution	} As used. See detail of work later.
„ Oxalicum -	1 in 200	Eusol -	
„ Picricum -	1 in 400		

*1% hardly killed *B. Coli* but 1 in 80 almost invariably does so after 2½ minutes contact.

THE MOST POTENT ANTISEPTICS—*continued.*

Flumerin	-	1 in 100	Liquor Cresolis Saponatus — cf. Ac.	
Formaldehydum	-	1 in 50	Cresylic	-
		(=5% 'Formalin')		
Gentian Violet	-	1 in 500	Mercurochrome	- 1 in 2,000
Hydrargyri Cyanidum	1 in 2,500		Malachite Green	- 1 in 1,000
Hydrargyri et Zinci Cyanidum (as paste)	33% paste		Potassii Chloras	- 1 in 50
Hydrargyri Iodidum (as Mercuric Potassium Iodide)	- 1 in 100,000		Potassii Permanganas	1 in 2,000
Hydrargyri Perchloridum	- 1 in 100,000		Saccharin Insoluble	- 1 in 40
Iodum	- 1 in 50,000		Sal Alembroth	- 1 in 90,000
			Sodii Salicylas	- 1 in 20
			Thymol	- 1 in 1,500
			Vesalvine S.	- 1 in 20

DETAILS OF OUR EXPERIMENTS.

Acetanilide. 0.25% Solution killed *B. Coli* in $2\frac{1}{2}$ minutes
0.125% did not.—W.H.M., 1914.

Acetone. 50% killed *B. Coli* in $2\frac{1}{2}$ minutes, 40% did not.

Acidum Aceticum. 7% kills *B. Coli* in $2\frac{1}{2}$ minutes, 5% does not kill.—W.H.M., 1914.

Active against *B. pyocyaneus* and successful clinically in infections with this organism, cf. Specificity in Antiseptics, *antea*.

Acidum Acetyl-Salicylicum.—Saturated Solution did not kill *B. Coli* in 30 minutes. R. Stockman states: A solution of strength 1 in 250 does not stop yeast fermentation, hence any antifermentative or antibacterial action must only occur when the Salicylic Acid is split off (Salicylic Acid 1 in 2,000 inhibits fermentation entirely and 1 in 5,000 greatly delays it).—B.M.J., i./13,598.

Acidum Arsenicum. 1% of Arsenic Anhydride did not kill *B. Coli* in $2\frac{1}{2}$ minutes.

Acidum Arseniosum. 2% of Arsenious Anhydride did not kill *B. Coli* in $2\frac{1}{2}$ minutes.—W.H.M., 1914.

Acidum Benzoicum. 0.2% killed *B. Coli* in $2\frac{1}{2}$ minutes.

Acidum Boricum. 1 in 25 (Saturated Solution) did not kill *B. Coli* in $2\frac{1}{2}$ or 30 minutes—and did not kill *Staphylococci* or *B. Typhosus* in 2 minutes.—W.H.M., *Expt.*, 1914. In no sense a disinfectant, but used in sufficient quantity it is a food preservative. The figure necessary for milk preservation is variously stated; 1 in 500 has been used, cf. Milk Preservation. 4% is usually employed as douche for the eyes and vagina and as mouth-wash.

Acidum Cacodylicum. 10% Sol. did not kill *B. Coli* in $2\frac{1}{2}$ minutes.

Acidum Camphoricum. 0.5% (Limit of Solubility) did not kill *B. Coli* in $2\frac{1}{2}$ minutes.—W.H.M., 1914.

Acidum Carbolicum. (see also "Lancet" and Rideal-Walker Coefficients, *antea*). 1.1% killed *B. Coli* in $2\frac{1}{2}$ minutes; 0.7% killed in 30 minutes, not in $2\frac{1}{2}$ minutes.

Liquid Phenol (10% water added) is caustic and anæsthetic. 1% is used as vaginal injection, mouth-wash and gargle.

Solution 1 in 20 is germicidal for B. Tuberculosis.—L. i./02,758.

The activity of this disinfectant on B. Coli is only slightly reduced by fæces and urine.—Hewlett. Alcohol diminishes activity of Carbolic Acid. Most Carbolic soaps are useless as disinfectants.—L. Cf. Glycerin in conjunction with Carbolic Acid.

Acidum Chromicum. $2\frac{1}{2}\%$ killed *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1914.* Also kills *Staphylococci*. This strength is used for ulcerated gums.

Acidum Cinnamic. 1 in 1,250 prevents yeast growth, but 1 in 2,000 does not.—*R. Stockman.*

Acidum Citricum. 8% killed *B. Coli* in $2\frac{1}{2}$ minutes. 4% killed in 30 minutes, not in $2\frac{1}{2}$ minutes.—*W.H.M., 1914.*

Acidum Cresylicum. 0.5% killed *B. Coli* in $2\frac{1}{2}$ minutes, 0.3% did not kill. Cf. *antea* and *Liq. Cresolis Saponatus*.

Acidum Formicum. 5% Solution killed *B. Coli* in $2\frac{1}{2}$ minutes, 2% did not.—*W.H.M., 1914.*

A strong antiseptic, but it is less active than Formaldehyde in destroying spores. As a preservative in foods, its taste is better than Acetic Acid. 'Werderol' contains 0.14% of it, as also does 'Fructol'; 'Alacet' 50 to 60%.—P.J. ii./24, 474.

Acidum Hydrochloricum. The acidity of the gastric juice probably serves as a protection against typhoid and cholera. Boer found that from 1 in 200 to 1 in 1,350 was necessary to kill anthrax, diphtheria, glanders, typhoid and cholera organisms, indicating variable resistance of different "non-spore-bearing organisms."

Acidum Hydrocyanicum. (2% HCN). Does not kill *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1914.* Fumigation of trees and ships is practised with this acid.

Acidum Hypochlorosum. See *Dakin's Solution* and *Eusol* in this chapter, also Vol. I.

Acidum Iodicum. 1 in 2,500 is deodorant and preservative. 1 in 500 is used as mouth wash and for ulcers.

Acidum Lacticum. 1% of actual Lactic Acid or less killed *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1914.*

Acidum Malicum. Vide "Specificity in Antiseptics," *antea*.

Acidum Oxalicum. 0.5% Solution killed *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1914.* Addition of Oxalic Acid is stated to increase the disinfecting power of Phenols.

Acidum Picricum. 0.25% killed *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M.* 0.165% Solution has the same bactericidal powers towards 24 hours broth culture of *B. typhosus* as 1% Phenol, the Rideal Walker coefficient being exactly 6.—*H. L. Tidy, L. ii./15,604.*

Acidum Pyrogallicum. 1% did not kill *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1914.* 3% according to Rideal kills most organisms.

Acidum Salicylicum. 0.1% kills *B. Coli* in $2\frac{1}{2}$ minutes, 0.05% does not. (Saturated Solution is of strength 1 in 500). Must not be used to the eyes. 0.2% killed *B. Typhosus* in 2 minutes.

1 in 2,000 inhibits fermentation entirely, and 1 in 5,000 greatly delays it.—*R. Stockman.* Vide also "Specificity in Antiseptics," *antea*.

Acidum Sulphuricum. 0.5% Dilution killed *B. Coli* in 2½ minutes, 0.1% did not.—*W.H.M.*, 1914. 0.05% stated to be fatal to *B. Cholerae* after 15 minutes contact.—*Rideal*.

Acidum Sulphurosum. 1% of the Off. 5% Acid killed *Staphylococci* and *B. Typhosus* in 2½ minutes.—*W.H.M.*, 1914.

Gaseous sulphurous Acid was until recently much used to disinfect rooms. The gas, however, is not powerful enough to kill *Anthrax* spores.

It was found that *B. Coli* and *S. Pyog. Aureus* were killed in 24 hours in a sealed room into which 20 ounces of SO_2 were passed. *B. subtilis* spores were not killed. *R.* mentions that a Bisulphate and Bisulphite together would be useful as they liberate SO_2 on moistening, thus: $\text{NaHSO}_4 + \text{NaHSO}_3 = \text{Na}_2\text{SO}_4 + \text{H}_2\text{O} + \text{SO}_2$.

Acidum Tannicum. 2% Solution did not kill in 2½ minutes. 40% Solution did not inhibit fungoid growth.—*W.H.M.*, 1914

Acidum Tartaricum. Vide "Specificity in Antiseptics," *antea*.

Acidum Trichloraceticum. 1 in 500 solution failed to kill *Staphylococci* and *B. Typhosus* in 2½ minutes. In throat affections 1 in 1 or 1 in 2 of Glycerin is astringent. 1 in 4 on a tampon with endoscope in gonorrhœa has been used. Less painful than Silver Nitrate.

Acridavine. The antiseptic power of this substance has been the subject of discussions, *v. Vol. I.*, p. 301, *et. seq.*

We found that 1 in 20 Solution did not kill *B. Coli* in 2½ minutes but 1 in 100 killed in 30 minutes.—*W.H.M.*, *Expt.*, 1921.

Alcohol. 70% killed *B. Coli* in 2½ minutes. 35% did not.—*W.H.M.*, 1914. It is not in itself reliable as an antiseptic.

The maximum efficacy as a disinfectant is obtained with Alcohol of 70% strength. Stronger Alcohol does not penetrate Albumin so readily and is, therefore, not so active as a germicide.

Alcohol Isopropylic. 30% killed *B. Coli* in 2½ minutes.—*W.H.M.*, 1925.

Allantoin. Saturated solution did not kill *B. Coli* in 30 minutes.—*W.H.M.*, 1921.

Allyl iso-sulphocyanidum. See *Oleum Sinapis Essentiale*.

Allyl Sulphide. 1 in 100 in a Saponaceous Solution killed *B. Coli* in 2½ minutes. Less dilutions failed to kill. Further 1 in 500 killed in 30 minutes. *C.A.* Coefficient is approx. 2. A simple Aqueous Sol. cannot be used in sufficient strength.—*W.H.M.*, 1914.

Alumini Chloras. 2½% Solution kills *B. Coli* in 30 minutes but not in 2½ minutes.—*W.H.M.*, 1914.

Ammonia. 1% of Ammonia did not kill *B. Coli* in 2½ minute.—*W.H.M.*, 1914. 0.5 Cc. of strong solution of Ammonia in 600 Cc. of Normal Saline killed *B. typhosus* and *B. cholerae* and partially *B. Coli* and *M. pyogenes aureus* in 4 hours. In the case of cholera the germicidal effect takes place in a few seconds.—*Hewlett*.

Antimonii et Potassii Tartras. 5% solution did not kill *B. Coli* in 2½ minutes.—*W.H.M.*, 1914.

Argenti Nitras. 1 in 2,000 solution killed *B. Coli* in 2½ minutes.—*W.H.M.*, 1914.

Lotions, Eye Drops, and Urethral Injections 1 in 1,000 up to 1 in

500. In eye work is more penetrating and active than the organic silver compounds on the market (see Text).

Boer found that from 1 in 4,000 to 1 in 20,000 killed anthrax, glanders, diphtheria, cholera, and typhoid organisms in 2 hours—i.e., a very variable resistance by different non-spore bearing bacteria.

Organic Silver Compounds. See Vol. I., p. 177.

Arsamin. 10% solution did not kill *B. Coli* in $2\frac{1}{2}$ minutes.

Arsenic. See *Acidum Arsenicum et Arseniosum*.

Aspidiodine (suspension in water). 1 in 75 killed *B. Coli* in $2\frac{1}{2}$ minutes but not 1 in 100.—W.H.M., 1925.

Auramine.

Auramine of Commerce is the Hydrochloride of Tetramethyl-diamino-diphenyl-ketanimine. It restrains the growth of Anthrax in dilution of 1 in 5,000, but on occasions 1 in 10,000 has killed. This body, in common with other Coal Tar dyes, does not possess a high Phenol Coefficient, but the Rideal-Walker method according to Browning, Renshaw and others, is probably not suitable for indicating the value of an antiseptic applied to the human body, since undoubtedly Auramine exerts far more antiseptic action in cases of sepsis than solutions of Carbolic Acid which can be tolerated. With paramæcium method, Phenol 1 in 500 kills within 15 minutes, but not completely 1 in 600, whereas Auramine 1 in 20,000 kills in 15 minutes. Aqueous solutions should not be kept for any length of time, since a slow hydrolysis occurs, the -imido group it contains becomes a ketone group with the formation of the insoluble Michler's ketone. It is stated that in bone sup-puration Auramine is superior to any other antiseptic.

See also our Vol. I., p. 322, and Coal Tar Dyes as Antiseptics this Vol., p. 265.

Our own experiments showed 1 in 500 Solution killed *B. Coli* in $7\frac{1}{2}$ minutes but an aqueous solution strong enough to kill in $2\frac{1}{2}$ minutes could not be made—cf. Glauramine below.

Glauramine equivalent to 1 of Auramine in 100 killed *B. Coli* in $2\frac{1}{2}$ minutes, while 1 in 150 failed to kill.—W.H.M., Expts., 1925.

Auri Cyanidum. 1 in 2,000,000, according to Koch, of $\text{Au}(\text{CN})_3$ dissolved in Potassium Cyanide checks growth of *B. Tuberculosis*.

Borates and Boric Acid. See *Acidum Boricum*.

Brilliant Green. 1 in 100 killed *B. Coli* in $2\frac{1}{2}$ minutes; 1 in 750 killed in 30 minutes, but not 1 in 1,000.—W.H.M., Expt. 1921.

Bromum. 1 in 20,000 killed *B. Coli* in 30 minutes, 1 in 8,000 $2\frac{1}{2}$ minutes.—W.H.M., 1914. Was found by Koch, to be the most powerful of all destructives to Anthrax and Tubercle bacilli.

Calci Hydraz (Slaked Lime) is not an antiseptic of any note.

Calci Permanganas. See *Potassii Permanganas*.

Carbonis Bisulphidum. Antiseptic, but odour and inflammability prevent its use.

Chlorinum 1 in 75,000 kills *B. Coli* in $2\frac{1}{2}$ minutes.—W.H.M., 1914. A cold saturated solution of Chlorine Water contains 0.634% by weight. (The activity of chlorine water probably owes its power to Hypochlorous Acid.)

'Chlorine Gargle,' which contains about 0.125%, is a potent antiseptic against *Staphylococcus pyog aureus* and other organisms.

Suitable for treating drinking water. No potable water would be likely to contain more than a small fraction of the number of cholera vibrios introduced into different waters used experimentally in the investigation in question (ranging from about 1,000 to 18,000 per Cc). It was concluded that most waters would be freed from cholera vibrios, if treated with 1 cf chlorine per million for 15 minutes.—L. ii./10, 1213; cf Vol. I., p. 45, and Iodine in Natural Waters Chapter, this Vol.

cf. also Eusol, this Chapter.

Ammonia increases the germicidal effect of bleach solutions. *Ammonium Chloride* has, however, no value. *Chloramine* is suitable for small dose and long contact periods.—*J. Race, L. ii./24,577.*

Chloroformum. 0.5% solution kills *B. Coli* in $2\frac{1}{2}$ minutes, 0.2% does not.—*W.H.M., 1914.* Our experiments showed further that 0.2% did not kill *Staphylococci*, nor *B. typhosus*.

Chlorphenols.

Tested on *B. Coli* *m*-chlorphenol showed the strongest antiseptic action, *p*-chlorphenol being weaker; and the ortho-compound the weakest. On *Staphylococcus aureus* *p*- and *m*- were about equal, being stronger than ortho-. The lethal dose for rabbits for the *o*-, *m*- and *p*- were 120, 65, 65 mgr. respectively.—*Arch. Exp. Path. Pharm., '26,60, per, B.C.A., '26, A.756.*

Chromates. See *Acid Chromic*.

Cinchonidine Sulphate, saturated solution, did not kill *B. Coli* in 30 minutes.—*W.H.M., 1921.—cf. Quinine Salts.*

Colloidal Solutions of Copper, Gold, Mercury, Platinum, Selenium and Silver were tested after $2\frac{1}{2}$ minutes, 30 minutes and 16 hours contact with *B. Coli*. With the exception of Mercury, which killed at $2\frac{1}{2}$ minutes, none had any power at $2\frac{1}{2}$ and 30 minutes. After 16 hours Silver and Gold (electrically made) inhibited growth. Gold (chemical), Platinum, Copper and Selenium did not inhibit.—*W.H.M., 1914.*

Colloidal Iodine E.P. diluted 1 in 100, kills *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1921.*

Collosol Argentum (*cf. Vol. I., p. 385*), is stated to kill *B. Coli* in 10 seconds.

Copper Salts. See below.

Creosote (Merson). 1 in 350 killed *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1914.* 1 in 150 is used in phthisis, &c., see text.

Crystal Violet. 1 in 100 did not kill *B. Coli* in 30 minutes.—*W.H.M., 1921.*

Cupric Chloride. *Kraemer* has advised for treating water 1 in 5,000. Is a stronger antiseptic than copper sulphate for the treatment of water supplies. A solution containing 1 of copper in 5,000 will kill *B. Typhosus* in slightly over an hour and *B. Coli* in an hour. (*Staphylococcus pyogenes aureus* is killed in less than two hours by a 1 in 7,000 copper sulphate solution.—*J. Sanitary Inst., 1904*).

1 in 100 killed *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1929.*

Cupri Sulphas. 1% killed *B. Coli* in 30 minutes but not in $2\frac{1}{2}$.—*W.H.M., 1914.* 1% is used for irrigation, see *Vol. I., Text.*

Dakin's Solution (diluted 1 in 6), 1 in 20,000 killed *B. Coli* in $2\frac{1}{2}$ minutes, 1 in 50,000 killed in 30 minutes. Tested same day as made—*W.H.M., 1921.*

Diffusol. This *Lysol* equivalent was highly spoken of for its diffusible power in the *Hunterian Oration, 1915, cf. Vol. I., p. 32.*

1 in 100 killed *B. Coli* in $2\frac{1}{2}$ minutes.—*W.H.M., 1921.*

Ethyl Iodidum. Readily destroys *B. Tuberculosis*. (*R.*)

Eucalyptol. See *Olea Essentiaia, Table of Coefficients.*

Eusol. 1 in 2,000 killed *B. Coli* in $2\frac{1}{2}$ minutes and 1 in 7,000 in 30 minutes. This was the result of trial same day as made. It deteriorates greatly on keeping. In a second expt. with Eusol 2 days old, 1 in 2,000 did not kill in $2\frac{1}{2}$ mins., nor did 1 in 6,000 in 30 minutes, but 1 in 3,000 did.—W.H.M., 1921.

Flavine. The antiseptic power of this substance or its absence has been much discussed, see Vol. I., p. 301, and Acriflavine, *antea*.

Flumerin (cf. Vol. I., p. 478). 1% killed *B. Coli* in $2\frac{1}{2}$ minutes, while 1 in 200 failed to kill.—W.H.M., 1925.

Fluorinum. More active than Chlorine. Fluorides and Silico-fluorides (cf. Salufer) are antiseptic. Fluoric Acid and Ammonium, Potassium and Sodium Fluorides are used in the brewing trade. 0.3% will prevent the acidity of butter. (R.). cf. *Specificity in Antiseptics*.

Formaldehyde 2% (=5% Formalin) kills *B. Coli* in $2\frac{1}{2}$ minutes. 1% Formaldehyde does not kill in $2\frac{1}{2}$ minutes.—W.H.M., 1914, but a small proportion inhibits growth. Formaldehyde, it would appear, is a slowly acting germicide. Cf. our Experiments under Hexamine, this Vol. Kingzett and Woodcock, for example, found that when incubated in the ordinary way it has a coefficient 0.38, while if allowed to act for $1\frac{1}{4}$ hours it is more potent than Phenol. Similar, and even more marked results would, we think, be obtained with many antiseptics. 1 to 2% is suitable for wounds, instruments and rooms. As deodorant, 5 or 10% is sufficient.

Its use as milk preservative in Great Britain is forbidden. For detection in Milk, v. Milk Preservatives.

10% solution is useful for disinfecting human discharges. Tubercle bacilli in sputum are stated to be killed by 5% solution in 1 hour.

It probably owes its antiseptic power to the ease with which it abstracts oxygen and becomes Formic Acid, a process which causes the breakdown of organic matter.

Fumigation of Rooms.

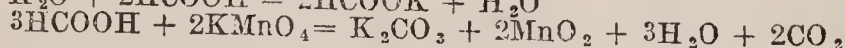
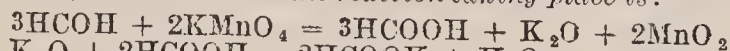
Hewlett says Formaldehyde is probably more active than Sulphurous Acid. Kenwood concluded from fumigation by Formaldehyde and by 1% Sublimate Spray, there was little to choose between these. Washing the rooms with soap is important. He recommended mixing 142½ Gm. of Permanganate and 285 Gm. of Formalin in a metal tray 7 inches in diameter and 3 to 4 inches deep—heat is generated and Formaldehyde escapes.

Formanganate Disinfecter. Consists of 16 ounces of 40% Formaldehyde solution and a box of two briquettes, made with 15% Portland Cement, each of 120 Gm. Permanganate for 1,000 cub. ft. space. Warmth—at least 65° F.—and moisture 60 to 65% humidity, are essential.

An apparatus may be improvised. 8 ounces of Permanganate is required for each pint of Formalin Solution per 1,000 cubic ft.

Suspend wet sheets to damp the air. There must be no live fire or flame in the room.

J. Rutherford Hill thinks the reaction taking place is:—



Alternatively evaporate Formalin in an open vessel over a Bunsen or spirit flame.

For disinfecting books.—Formalin vapour is useless. Expose the books at 180°—190° C. in a hot air steriliser for an hour or two on three successive days.

0.8% of Formaldehyde kills *B. Diphtheriae* in 10 minutes, *B. Dysenteriae* in 60 minutes, *B. Typhosus* in 40 minutes. *Staphylococcus pyogenes albus* in 60 minutes, *Staphylococcus pyogenes aureus* in 40 minutes. 2% Formaldehyde killed *Staphylococcus pyogenes albus* in 30 minutes, *B. Dysenteriae* in 40 minutes, *Staphylococcus pyogenes aureus* and *B. Typhosus* in 20 minutes. 4% Formaldehyde killed all the non-sporing organisms investigated in less than 10 minutes except *B. Dysenteriae* and *Staphylococcus pyogenes aureus*, which, however, were killed after 10 minutes.—*B.M.J.E.* ii./08,7.

Gentian Violet.—A 0.2% solution killed *B. Coli* in 2½ minutes.

Glauramine, see **Auramine**.

Glycerin is preservative for vegetable preparations (cf. *Glyce-tracta*), but, as anticipated, our experiments gave + with pathogenic organisms.

J. L. Moir has suggested the use of **Carbolised Glycerin** as an **injection in labour**, as a means of preventing puerperal infection. **The exact proportion of Phenol in Glycerin to employ is open to discussion.**

The injection would be given into the vagina before labour, prior to any manipulative or operative interference, and would be repeated at the conclusion. It would appear that if the tissues can be kept in constant contact with a viscous substance like Glycerin, impregnated with a potent antiseptic, during the whole of labour the chances of infection from the outside may be reduced.

The rationale depends on the hygroscopic action of Glycerin decreasing the causticity of the Carbolic Acid, so that the tissues are not devitalised, and at the same time the Carbolised Glycerin acts as a barrier to external infection.

The proportion of Phenol should be efficacious, but not injurious to the delicate membranes and without possibility of causing shock, either to the mother or offspring.

Again, in the test-tube, Glycerin may hinder the potency of the Phenol, though this would appear a relatively negligible issue. It will be recalled that *H. P. Goodrich* (*B.M.J.* i./17,647) stated that the presence of Glycerin (in mouth washes) more or less completely destroys the potency of Phenol, Thymol, Mercuric Chloride, etc. Personally, we think the statement too sweeping. We recently (1929) determined, however, that the **Bactericidal effect is hindered to an extent, i.e.,** between 1 in 40 and 1 in 50 in Glycerin killed *B. Coli* in 2½ minutes, while 1 in 120 in water does the same.

We doubt whether the theoretical, or commonly asserted, power of Glycerin to reduce toxic effect can be sufficiently relied on in the method of childbirth advocated. The only guides available as to safe proportion to employ, are the various (aqueous) vaginal injections of the hospitals, e.g., King's College, and the Samaritan Hospital, 1 in 60, and the Chelsea Hospital for Women, 1% approx., and we should not care to advocate a 1 in 40 solution (or stronger) in Glycerin for the purpose.

It may be added that *H. J. Phillips* (*L.* ii./25,1229,1307) draws attention to the useful lymphagogue action of Glycerin in labour, with the addition of Iodine.

It seems probable that Carbolised Glycerin of 1% **strength** would be safe and effective clinically.

The following is also relevant:—

Glycerin is an **ideal antiseptic** in the sense of being less fundamentally toxic for leucocytes, as representative tissue cells, than for a typically resistant bacterium like the staphylococcus. A new antiseptic characteristic is indicated—the bacterial indifferent zone of cyto-bacterial activity—present in antiseptics possessing greater toxicity for tissue cells than for bacteria, and absent in antiseptics possessing greater toxicity for bacteria, which affords a criterion for the selection of useful antiseptics and the rejection of those likely to do more harm than good. In a study of the direct action of glycerin on various bacterial types met with in the genito-urinary tract, it is established that glycerin is but **feebly bactericidal** in comparison with its **markedly antiseptic character**.

Glycerin inhibited growth of *Gonococcus* in subculture in 13–30 minutes and of *Streptococcus* in about 4 hours.

No untoward effects, such as necrosis or sloughing have ever been observed following its intra-uterine use.

The time limits of its bactericidal and of its antiseptic responses to a number of bacteria are indicated. The **streptococcus succumbs** comparatively early to the bactericidal action of glycerin. These new facts make glycerin

one of the most interesting and ideal antiseptics, and indicate for it a sphere of even greater usefulness in the treatment of inflammatory conditions.—A. Comp-ton, *L. ii.*/26,326.

Glycerin used for controlling hæmorrhage in Caesarean Section, and promoting drainage of the uterus during the puerperium. After removal of placenta the cavity is swabbed out with Glycerin.—M. Salmond, *L. ii.*/29,660.

Gualacol is stated to have greater power than Phenol, i.e., as 5 : 2.

Hexamine—10% did not kill *B. Coli*, but less amount inhibits growth gradually in acid solution.—W.H.M., 1914. (cf. Hexamine, this volume, and Vesalvine 'S').

Hydrargyri Ammonio-Chloridum ((Sal Alembroth). 1 in 90,000 killed *B. Coli* in 2½ minutes, 1 in 120,000 did not.—W.H.M.

Hydrargyri Cyanidum. 1 in 2,500 killed *B. Coli* in 2½ minutes, 1 in 3,000 did not.—W.H.M., 1914. As gargle 1 in 10,000 is used. We should prefer 1 in 5,000 at least. For fibroid rhinitis tampons impregnated with 1 in 2,500 have been used. Extremely poisonous.

Hydrargyri et Zinci Cyanidum. We found 2 minutes with the 33% paste (q.v.) killed *Staphylococci* and *B. typhosus*. As first dressing to wounds 3% gauze and wool and paste are non-irritant.

Hydrargyri Iodidum Rubrum used as Mercuric Potassium Iodide. 1 in 100,000 killed *B. Coli* in 2½ minutes.—W.H.M. For hands 1 in 4,000, Collyrium 1 in 5,000, wounds 1 in 7,000, vaginal douche 1 in 10,000. Not so irritant as the Perchloride.

Hydrargyri Oxycyanidum. 1 in 1,000 or more kills *B. Coli* and *B. Typhosus*. As pigment in syphilis 0.2 to 0.6%.

Hydrargyri Perchloridum 1 in 100,000 killed *B. Coli* in 2½ minutes; 1 in 250,000 failed to kill in 15 minutes.—W.H.M. The most potent antiseptic. Its intensity is increased by presence of Hydrochloric Acid, e.g., 1 in 500 with 1 in 120 of acid, for disinfecting excreta. (Woodhead says ½% Hydrochloric Acid.) It is precipitated by soluble organic matter. For eye, nose and mouth lotion 1 in 4,500, vagina 1 in 10,000. For linen, rooms, gynecologists' hands and superficial wounds 1 in 10,000 to 1 in 1,000. cf. Statements, Vol. I., p. 467, also this vol. p. 263.

The power (on *B. Anthracis* spores) of Equimolecular Solutions of this salt, the bromide and the cyanide, is stated to be in this order—corresponding to their degree of dissociation in solution.

Hydrogenii Peroxidum (10 Vol.). 12% did not kill *B. Coli* in 2½ minutes.—W.H.M., 1914. Is variously employed: even the strong official solution may be employed on mucous membrane. It is contained in Sanitas q.v. Hyperol is a compound of H_2O_2 and Urea, rendered stable by a trace of Citric Acid.

Iodine. 1 in 50,000 kills *B. Coli* in 2½ minutes.—W.H.M., 1914. It is employed as a first aid dressing and to sterilise catgut (q.v.). Iodine is potent against other organisms, but unfortunately, to check *B. Anthracis* once established in the human body 12 Gm. of Iodine would have to be in constant circulation in the system. (Koch.)

Consult also the complete résumé, Vol. I., p. 518.

T. Maben and J. S. White found the killing power of iodine in the form of Alcoholic or Aqueous solution on *B. Typhosus* is at least four

times more powerful than that of a solution of cartolic acid of the same strength.—C.D. Jany, 30, 1915.

Iodoform. A paste of Iodoform will kill *B. Coli* and *B. Typhosus* in $2\frac{1}{2}$ minutes, but not *Staphylococci* invariably. It is used as a bladder injection with glycerin, also as a dusting powder and wool dressing.

It has been stated, and is probably true, that Iodoform crystals may be infected with adherent organisms, and the same remarks apply to Corrosive Sublimate (dry).

'Iodo-Ray.'—1 in 10 Solution did not kill *B. Coli* in $2\frac{1}{2}$ minutes.—W.H.M., 1929.

Iron. Frankland proved that Metallic Iron is destructive to bacteria. Ferrous Sulphate is stated to be mildly antiseptic. Ferric Sulphate and Chloride check fermentation and bacterial growth.

Lead Salts. Are antiseptic. A proportion of 2.0 Gm. per litre is stated to preserve broth.

Liquor Aluminii Acetatis P.G. kills *B. Coli* in 30 minutes but not in $2\frac{1}{2}$ minutes.—W.H.M., 1914.

Liquor Carbonis Detergens. We found a 2% solution killed *B. Coli*, *B. Typhosus* and *B. Anthracis* in $2\frac{1}{2}$ minutes. A remedy in skin affections, strength used 1 in 8 up to 1 in 160 (see Text).

Liquor Cresolis Saponatus. 0.5% killed *B. Coli* in $2\frac{1}{2}$ minutes.—W.H.M., 1914. C.A. Coefficient 1.5. For midwifery 1% is usually employed.

Liquor Formaldehydi Saponatus. cf. Formaldehyde.

Lister's Antiseptic. See *Hydrargyri et Zinci Cyanidum*.

***Lysoform.** 2% kills *Staphylococci* and *B. Anthracis*, but at least 10% is necessary for *B. Coli* and *B. Typhosus*.—W.H.M., 1912. It is employed for wounds and irrigation. Contains Formaldehyde. Lathers with water. Non-poisonous.

Magnesii Sulphas. 20% sol. did not kill *B. Coli* in 30 minutes.

Malachite Green. 1 in 1,000, but not 1 in 2,000, killed *B. Coli* in $2\frac{1}{2}$ minutes.—W.H.M., 1921.

Malourea.—1% failed to kill *B. Coli* in 30 minutes.

Mercuric Chloride. See *Hydrargyri Chloridum*

Mercutic Cyanide. See *Hydrargyri Cyanidum*.

Mercurochrome. The compound made by the author, in 1 in 2,000 Solution killed *B. Coli* in $2\frac{1}{2}$ minutes.—W.H.M., 1925.

Methylene Blue. 1 in 100 did not kill *B. Coli* in $2\frac{1}{2}$ minutes; 1 in 750 killed in 30 minutes but not 1 in 1,000.—W.H.M., 1921.

Naphthalene.—A paste kills *B. Typhosus* but not *Staphylococci* invariably.

Enemata of 8 grains have been used. Parasitic in scabies, 10 to 20% solution in oil. Used as deodorant in closets, but not a disinfectant.

Naphthol β . A paste we found will kill *B. Typhosus* and *Staphylococci*. Oily Solution 10% has been used. This appears to be active.

Neutral Red. 1 in 100 did not kill *B. Coli* in $2\frac{1}{2}$ minutes nor in 30 minutes.—W.H.M., 1921.

Nicotinae Tartras. 10% solution kills *B. Coli* in 30 minutes, but not in $2\frac{1}{2}$ minutes.

Novarsenobillon. 1 in 100 did not kill *B. Coli* in 30 minutes.

Oleum Allii. See Allyl Sulphide.

Oleum Sinapis Essentiale. 0.1% did not kill *B. Coli* in 300 minutes.—*W.H.M.*, 1914.

Oils Essential. See Vol. I., p. 600, and the Chapter in this Vol.

Oxygen Nascent e.g., from Permanganate, is antiseptic.

Ozone in the dry state has little action on micro-organisms.

***Paraform.**—A paste with water kills *Staphylococci* and *B. Typhosus* in 2 mins. The vapour (Formaldehyde) sterilises instruments and catheters. Tablets (15 grains) are made for fumigation of rooms. 20 of these disinfect 1,000 cub. ft.

Persulphates are antiseptic. **Ammonium Persulphate.** 1 to 2% kills *Cholera* organisms and others in a few minutes.

Sodium Persulphate. 2% solution did not kill *B. Coli* in 300 minutes.—*W.H.M.*, 1914.

Phenazonum. 10% solution did not kill *B. Coli* in 2½ minutes.

Potassii Bromidum. 20% did not kill *B. Coli* in 30 minutes.

Potassii Chloras. 2% kills *B. Coli* in 2½ minutes; 1% kills *B. Coli* in 30 minutes, but not in 2½ minutes.—*W.H.M.*, 1914.

Potassii Permanganas. 1 in 2,000 kills *B. Coli* in 2½ minutes; 1 in 5,000 does not, but does so in 30 minutes.—*W.H.M.*, 1914. A good deodorant. In presence of organic matter, however, its power is reduced by it oxidising the organic material.—(*Calcium Permanganate* approximates the Potash Salt in potency.)

In gonorrhœa 1 in 1,000 gargle and vaginal douche 1 in 5,000 of either salt are employed (cf. Vol. I., p. 553). Bousfield found sewage control in his experiments give 239 colonies in 0.00001 Cc. against sewage with 1 in 5,000 permanganate 99, 1 in 2,500 had 23, and 1 in 1,000 one colony—the time of contact being 12 hours. Further work showed that the time element is of no importance—results after 5 minutes' contact were as good as after 4 hours. A source of error in the Rideal-Walker method was overcome by diluting the disinfectant after 12 hours' contact to 1 in 100,000 of the strength at which it had been allowed to act for the purposes of the experiment before making the cultures. The general conclusion was that **1 in 1,000 is efficient** and that if such a mixture of permanganate and sewage is deodorised it is also sterilised.

Pyrogallol. See Acid Pyrogallic.

Quinidine Sulphate, sat. sol. did not kill *B. Coli* in 30 mins.—1921.

Quininæ Hydrochloridum. In experimental gas gangrene found to be more effectual than phenol—especially active in a menstruum of pus.—*K. Taylor*, L. ii./15,538,977. cf. *Specificity in Antiseptics*.

Quininæ Hydrochloridum Acidum. 10% Solution did not kill *B. Coli* in 2½ minutes.—*W.H.M.*, 1914.

Quininæ Sulphas. 1 in 500 Solution stated to be necessary for killing effective organisms (in a common cold). See also Vol. I.

Quininæ Sulphas Acidus, stated to have C.A. Coefft. 0.5. It will inhibit growth of fresh Typhoid cultures in 1 in 30,000 dilution.—

Resorcin. 3.5% killed *B. Coli* in 2½ minutes, 1% did not kill in 30 minutes.—*W.H.M.*, 1914.

Is non-irritant on mucous membrane, e.g., bladder, 5% is used. As collyrium 2%, as enema 0.5%. See also Text.

Saccharin, Insoluble. 0.25% killed *B. Coli* in 2½ minutes.

Saccharin, Soluble.—5% did not kill *B. Coli* in 30 mins.—1914.

Sal Alembroth. See **Hydrargyri-Ammonio-Chloridum**.

Scarlet Red (water soluble) 1 in 50 did not kill *B. Coli* in 2½ or in 30 minutes.—*W.H.M.*, 1921.

Sedasprin (Suspension in water). 1 in 50 killed *B. Coli* in 2½ minutes but not 1 in 75.

Soap. Though not giving a high Carbohc coefficient is generally acknowledged to be germicidal. We tried a 2% solution which was useless on *B. Coli*, *B. Typhosus* and *Staphylococci*.

Sodii Chloridum. 33% Solution did not kill *B. Coli* in 30 minutes.—*W.H.M.*, 1914.

Sir A. E. Wright says 5% will arrest the growth of pyogenic organisms—*L. ii.*/15, 1063.

It is not an active bactericide. Brines to be used for salting and pickling have been found to be contaminated. In the case of butter and cheese serious damage is often done by the use of contaminated salt.—*P.J. i.*/25, 696.

Sodium Fluoridum. Active against *staphylococcus aureus* and *strepto. pyogenes* and *B. pyocyaneus*, and fairly so against *B. aerogenes capsulatus*. cf. *Specificity in Antiseptics, antea*.

Sodii Metabisulphis. 2.5% in Glycerin kills *Staphylococci*, but did not kill *B. Typhosus* in 2½ minutes.—*W.H.M.*, 1914. A pigment this strength has been used for thrush.

Sodii Persulphas. See **Persulphates**.

Sodii Salicylas. 5% killed *B. Coli* in 2½ minutes, 1% did not.—*W.H.M.*, 1914. A feeble germicide and antifermentative. It has almost no action on yeast or bacteria.—*R. Stockman*.

Sodii Sulphas Acidus. Has been used for water sterilising for Army use, but we were informed it may produce looseness of the bowels. One Antityphoid Tablet to the pint of water is stated to destroy *B. Typhosus* and *B. enteritidis* in 15 minutes. We found it killed *B. Typhosus* and *Staphylococci* in 2 minutes, in above proportion.

Sodii Sulphis. 1 in 500 we found did not kill *Staphylococci* or *B. Typhosus*.

Sodii Taurocholas. 20% sol. did not kill *B. Coli* in 30 mins., 1914.

Strychninæ Hydrochloridum. 2½% solution did not kill *B. Coli* in 30 minutes.—*W.H.M.*, 1914.

Sulphonal. 1 in 450 (saturated solution) did not kill *B. Coli* in 30 minutes.

Tar. See **Liquor Carbonis**.

Terpin Hydrate. 0.25% said to arrest Tubercle Bacilli.

Thorii Nitras. 1% killed *B. Coli* in 2½ minutes.—*W.H.M.*, 1914.

Thymol. 1 in 1,500 killed *B. Coli* in 2½ minutes, 1 in 3,000 kills in 30 minutes but not in 2½ minutes.—*C. A.* Coefficient 19 approximately.—*W.H.M.*, 1914. 1 in 800 is used as gargle. It is soluble 1 in 1,500 water and 1 in 200 glycerin.

Thymol Disinfectant. A potent germicide. *R.W.* Coefficient 8. *Vide Vol. I.*, p. 810.

Toluol (cf. *Benzol*, Vol. I., which it resembles). Did not hinder growth of *Staphylococci*.

Tooth-Pastes. The antiseptic values of some—the active samples have a coefficient of about 0.1.—P.R. '24,387.

Trikresol. C.A. Coefficient 2.5. 1 in 2,000 appeared to hinder *Staphylococci* and *B. Typhosus* which ultimately developed (in 600 hours). $\frac{1}{2}\%$ on the other hand, killed *B. Coli* and *B. Typhosus* but not *Staphylococci*. In general surgery $\frac{1}{2}$ to 1%. Eye wash 1 in 1,000 to 1 in 2,000.

Uranii Nitras. 5% killed *B. Coli* in 30 mins., but not in $2\frac{1}{2}$ mins., 1914.

Veronal, See *Malourea*.

Vesalvine 'S.' 5% killed *B. Coli* in $2\frac{1}{2}$ minutes. $2\frac{1}{2}\%$ killed *B. Coli* in 30 minutes but not in $2\frac{1}{2}$ minutes.—W.H.M., Expt., 1914.

Xylenois are more bactericidal than *Cresols*—they are obtained from blast furnace tars and are present only in small amount in ordinary Coal Tar. The cheaper disinfectants usually consist of *Creosote* and *Cresylic Acid* emulsified with *Resin Soap*.

A disinfectant with 35% *Xylenols* may have C.A. Coefficient 20 or over.

"	"	25%	"	"	"	"	"	"	15	"
"	"	20%	"	"	"	"	"	"	20	"

—A. C. Tait, C.D. ii./26,932.

Zinci Chloridum. The results of our tests showed that *Zinc Chloride* was not of much avail. 1 in 1,000 failed to kill *B. Typhosus* and *Staphylococci* in $2\frac{1}{2}$ minutes. 1 in 500 is an astringent lotion. It is very poisonous. A $2\frac{1}{2}\%$ Solution was found to destroy bacteria, but *Koch* found even 5% would not kill *Anthrax* spores.

Zinc Chloride salt of Aniline.

The salt $(\text{NH}_2\text{Ph})_2\text{ZnCl}_2$, was formed by intimately mixing *Aniline* and fused *Zinc Chloride*, was soluble 0.64% in water, and had greater bactericidal action than either *Aniline* or *Zinc Chloride*, efficiency being approx. in the ratio of 10 : $7\frac{1}{2}$: 2.—J.C.S., A. i./24,249.

Zinci Permanganas. 1 in 5,000 prevented growth of *B. Typhosus* and *Staphylococci*. Employed similarly to the *Potash Salt*. Absence of irritation is a feature.

Zinci Sulphanilas. 1% killed *Staphylococci* but did not kill *B. Coli* or *B. Typhosus*. 1 in 250 killed *Staphylococci*, but not others.

Zinci Sulphas. 2% killed *B. Coli* in 30 minutes but not in $2\frac{1}{2}$ minutes.—W.H.M., 1914.

Zinci Sulphocarbolas. $2\frac{1}{2}\%$ killed *B. Coli* in $2\frac{1}{2}$ mins., 1.25%—did not.—W.H.M., 1914.

Essential Oils have *Antiseptic Powers*.—v. p. 126.

Sunlight according to *Koch* will kill the *Tubercle Bacillus* in from a few minutes to 5 or 7 days, according to the thickness of the medium. Light is important for diminishing the number of bacteria.

Heat owes its bactericidal power to its coagulating effect on bacterial proteins. Moist heat is best because apart from its penetrating power it is well-known the protein in the dry condition coagulates at a much higher temperature than when moist.—Hewlett.

Filters. The 'Pasteur-Chamberland' or 'Berkfeld,' or similar apparatus of the porous candle type are efficient instruments.

IONTOPHORESIS.

Syn. KATAPHORESIS, MEDICAL IONISATION.

In the dissociation of a molecule of a substance—inorganic or organic in solution—the nascent particles of the elements are called ‘ions.’ They are charged with electricity and are in rapid motion. The + charged are called ‘Kations’ and those – charged ‘Anions.’ Various agencies in addition to electricity are capable of causing the splitting up of compounds with the formation of ions, *e.g.*, heat, light, and Rontgen Rays. Dilute solutions of substances contain free ions of the substances. Dilute Hydrochloric Acid can be electrolysed (split up) into its constituents Hydrogen and Chlorine which in their ionised condition appear at the poles of a battery, the Hydrogen at the **Kathode** (negative pole) and the Chlorine at the **Anode** (positive pole). On reaching their respective poles they lose their existence as ions. All solutions capable of conducting electricity probably contain molecules *already* dissociated.

When zinc and copper plates are in contact, *e.g.* by a wire, in dilute sulphuric acid, electricity passes across the junction from copper to zinc and then from zinc through the exciting liquid to the copper again.

The galvanic current passes through some conductors with little difficulty—silver and copper for instance, if pure and moderately thick, have extremely little resistance, whilst others, *e.g.*, Platinum and the element Carbon, especially if of very small cross section, cause a considerable amount of resistance and *ergo* heat—this in the case of Platinum is used in the galvanic cautery, whilst Carbon is employed to restrain current—*i.e.* as a rheostat.

Non-Electrolytes are substances not capable of conducting electricity, *e.g.*, pure water, aqueous solutions of Alcohol or Sugar, Benzene, and a large number of Organic Compounds. Nitrobenzene, Ethyl Nitrate, Chloral, are not electrolysed. Furthermore, Glycerin, Chloroform, Petroleum Jelly, do not dissociate electrolytes (*cf.* the relative non-toxicity of Glycerin of Carbolic Acid). A 5% Aqueous Solution of Phenol applied to an ulcer of the leg as a permanent dressing may prove most serious, whilst an Ointment of the same strength will make an excellent dressing. In aqueous electrolytic solutions the + and – ions are equally diffused, the + electricity of the one (metals) exactly neutralising the – electricity of the other.

The *Electrolytical Solution pressure*, *i.e.*, tendency of different metals to become ionised when in contact with a liquid varies with different metals, *e.g.*, in the case of:—

Zinc, Iron, Lead, *Hydrogen*, Copper, Silver.

The metals on the left have electrolytic solution pressure greater than H and those on the right. The former deprive H ions of their positive charges and thus displace H in an electrolytic cell. They dissolve in acids with evolution of hydrogen. In the voltaic cell of Zn, Cu and H_2SO_4 , the Zn by its high electrolytical solution pressure tends to form + charged Zn ions, and in doing so becomes – charged, the Cu has almost no tendency to become ionised and acquires a positive

charge.—Lewis Jones. In addition to these two classes Newth mentions a class midway termed half-electrolytes. The terms strictly apply to the actual liquids or solutions—it is, *e.g.*, the *aqueous solution* of sodium chloride which is the electrolyte.

Paul and Krönig in 1896 found that solutions of various antiseptics containing toxic ions in the same proportion are equally antiseptic. One gramme-molecule in 64 litres of either Mercuric Chloride or Bromide is more powerful than Mercuric Cyanide solution four times the strength, as Mercuric Cyanide undergoes less dissociation.

In **Kataphoresis**—introduction of medicaments into the tissues by ionisation—a movement of the electrolyte, comparable with osmosis, takes place under the current generally in the direction of its flow, *i.e.*, from + to – pole. Fluid can in this way be made to pass through porous diaphragms, *e.g.*, the skin, but the migration of the ions is a more important consideration.

The Kations (+ charged) travelling to the Cathode include H, Na, K, Li, Pb, Cu, Fe and Bi.

The ions of alkaloidal bases in solutions of their Salts are also set free at the positive pole and are therefore applied medically at the Anode. (Positive Pole.)

The Anions (– charged) carry this electricity to the Anode. They include most of the metalloids and non-metals, also the following groupings—OH, NO₃, ClO₃, C₂H₃O₂, SO₃, C₂O₄, PO₄.

These must, therefore, be introduced for medical purposes under the Kathode. (Negative Pole.)

The name ‘ion’ (a traveller) was given to these by Faraday. The Anions travel *against* (sometimes called *up*) the current, the Kations *with* (sometimes called *down*) the current.

The electrical capacity of the ions varies with the valency of the element. The ions of 1 gramme-molecule of hydrogen and all monovalent elements carry electricity equivalent to 96,550 Coulombs. Divalent ions carry twice the quantity and so on.

Kations. MONOVALENT OR UNIPOLAR KATIONS:—

H, NH₄, K, Na, Li, Ag, also Hg(ous) and Cu(ous).

DIVALENT:—

Mg, Ca, Fe(ous), Ba, Sr, S, Zn, Pb, also Hg(ic) and Cu(ic).

TRIVALENT.—Fe(ic), Al, Bi and Sb.

Anions.—MONOVALENT.—OH, F, Cl, Br, I, NO₃, ClO₃, C₂H₃O₂, and the Anions of all Monobasic Acids.

DIVALENT.—SO₄, SO₃, S₂O₃, CO₃, S (Sulphide), C₂O₄ and all anions of dibasic acids.

TRIVALENT.—PO₄ and other anions of tribasic acids.

The neutralising power is dependent on the valency, *e.g.*, a trivalent Nitrogen Anion requires three monovalent Hydrogen Kations for neutralisation. The halogens, as also Carbon, Sulphur, and Phosphorus show a variable valency.

The more a solution is diluted—up to a point—so much greater is the ionisation and rate of molecular conductivity.

Osmotic pressure is influenced by ionisation. It is in proportion, in the case of electrolytes, to the molecules plus ions in the solution. In the case of non-electrolytes the osmotic pressure is only proportional to the number of molecules.

The **rate of absorption** of Salts through animal membranes has been found to differ according to the proportion of contained ions. K, Na, and Li were absorbed about equally. NH_4 and Urea were absorbed more rapidly, Ca more slowly, and Mg slowest of all.

Of the Anions Cl is absorbed most rapidly, then Br, I, NO_3 , SO_4 in this order.

The **taste** of substances has by some been thought to be due to dissociation, *i.e.*, to the action of Ions on the tongue or nerve endings—*e.g.* the H ions in the case of Acids. A Hydrochloric Acid Solution of distinct acidity to the tongue is tasteless when neutralised by Potash.

A small amount of Sodium Acetate added to a dilute solution of Hydrochloric Acid diminishes its acid taste. This view is debated however

Crystalloid substances are either electrolytes or non-electrolytes—the former constitute the Salts, Acids and Bases—the latter consisting mostly of organic substances such as Sugar or Urea. They readily pass through animal membranes, *cf.* Vol. I., p. 361, and have a strong affinity for water. Their ions play an active part in the well-being of the organism.

The Mineral Constituents of the human body in the concentration in which they are present are almost completely dissociated—the remaining molecules (undissociated) are neutral electrically.

Colloid substances do not pass through animal membrane and their osmotic pressure is so low that they diffuse with utmost difficulty. The particles in a colloidal solution possess energy, part of which is potential and part kinetic, by reason of their electrical charge, their chemical combinations, etc.

Change from colloid to crystalloid in the organism and *vice versa* is continuously proceeding.

All crystalloids have the power of modifying the gelation of colloids, but only the electrolytes have the power of precipitating them. The precipitating power of the electrolytes varies. Mg, NH_4 , K, Na and Li increase in power of precipitation in this order, but the anions—Sulphate, Phosphate, Citrate, Tartrate, Chloride, Bromide, Iodide, and Sulphocyanate inhibit the action of the metallic ions, and the power to prevent the precipitation of Proteins also increases in this order. Thus the Sulphates increase in precipitating power from Mg to Li, and on the other hand Sodium Salts decrease in precipitating power from Sulphate to Sulphocyanate in the order given.

In the living organism it is well known that the salts are held fast with great force, and this is an analogue of the affinity exhibited between the salts and the Proteins. According to Pauli all the Protein constituents of the protoplasm enter into the composition of this substance only in combination with ions.

It is the general opinion that there is no sharp limit between solutions of crystalloids and colloids—all properties of the one are found in the other—the difference is only in degree. Colloids have enormous molecules, *e.g.*, those of Albuminoids, and hence their solutions have a feeble molecular concentration and feeble osmotic pressure.

The importance of acquiring knowledge of the osmotic pressure of the fluids of the body is evidenced in every day treatment, *e.g.*, in the use of 'Normal Saline Solution.' Application of pure water causing osmosis in mucous membranes is painful and the use of a too concentrated Saline Solution will cause blood corpuscles to part with their water and break up completely.

The readily diffusible substances Urea, Sugar, etc., are produced by decomposition of Protein or Carbohydrate during metabolism—these are fortunately non-electrolytes, they are ionised only very slightly or not at all—this is of the utmost importance to the organism.

All **Kations** precipitate protein. They increase more or less irritability of muscle and nerve,—they excite intestinal activity and increase blood pressure.

Anions dissolve protein (inhibiting the action of Kations in general). The Sulphates, Citrates and Tartrates precipitate protein because the anions are associated with the over-balancing properties of the metallic ions. They are therefore cathartics. But in the case of Nitrates, Bromides, Iodides, the anion predominates in effecting sedative action and decrease of blood pressure.

The cathartic and precipitating power run parallel in the previous type of substances.

It may be that organic compounds of metals, *e.g.*, Salvarsan, owe their properties to their decomposition with the giving off of the metal in ionized form and this may be the real value of colloidal preparations of metals and other powerful drugs.—Bayliss.

Application of Ionisation Medically.—

The introduction of medicamenta by ionisation brings about a substitution of the fresh ions for the ions of the organism. Hence caution is needed as to the purity of the substances, the strength of current used, and method of procedure. The quantity of drug caused to penetrate is strictly proportional to the magnitude of current and the duration of its flow.

Ionic Medication is easy of application, treatment is localised and it is relatively painless.

The Solutions are applied by means of a disc covered with a pad of a number of thicknesses of Lint or Absorbent Cotton Wool, or by a **Glass Cup Electrode**. This, the *active* electrode, is covered with a piece of pig's bladder, which is capable of allowing the ions to pass. The *indifferent* electrode is applied in any convenient situation.

The Unit of Electromotive Force is the *volt*. Resistance of a conductor is stated in *ohms*. Strength of Current is expressed in *ampères*. The *ampère* is the Current which an E.M.F. of 1 *volt* produces in a circuit where the resistance is 1 ohm,—for medical use the 1/1000 part, the *milliampère*, (*m.a.*) is the Unit or Standard. It is measured by D'Arsonval's Milliampère-meter.

The *Coulomb* is the unit of quantity of current—it is delivered by a current of 1 *ampère* in 1 second.

The density of the current used, $\frac{1}{S}$ (intensity divided by surface of the conductor) is important in medical use. 100 *m.a.* introduced by a surface of 1 sq. cm. will produce a different effect from the same current traversing 100 sq. cm.—as could easily be imagined, each sq. cm. in the last case being traversed by 1 *m.a.* in place of 100.

Electrical Energy or the power of doing work is measured in *joules*. One joule represents the energy expended in one second by one ampere with resistance of one ohm.

Strength of Current used :

One requires for ionising about 40 to 50 volts, which with a total resistance of 400—500 *ohms* will produce a current of 100 *m.a.*

$$I = \frac{E}{R} = \frac{50}{500} = 0.100.$$

(Ohm's Law : Intensity of Current is equal to E.M.F. divided by the Resistance or $C = \frac{E}{R}$)

A current of 30 to 40 *m.a.* as a minimum, 50 to 70 *m.a.* as an average and 100 to 150 *m.a.* as an exceptionally strong one may be taken as a rough index of the current to be used in the treatment of a large joint, such as a knee, with Salicylic ions, which require a stronger current than most other ions. In the case of the last strength a quarter of an hour ought to be occupied in reaching this. If the ions are penetrating into the tissue, the hand of the milliampèremeter will be noticed to gradually rise and then become stationary, but should the

hand be seen to recede, this will signify that the ions are not penetrating properly, but are gathering on the surface and forming a resistance to the current. Abrasions of the skin should be first covered with a small piece of some non-conductor before applying the electrode.—Lewis Jones.

Resistance of the Body may be calculated by Ohm's Law from the galvanometer reading and the electromotive force of the cells—e.g., with 6 Leclanché cells the E.M.F. being 9 volts, if the current through the patient be 4 m.a., the resistance may be found thus:—

$$R = \frac{E}{C} = \frac{9}{0.004} = 2,250 \text{ Ohms.}$$

In employing the continuous current from the electric mains in place of batteries or accumulators secondary circuits of high resistance are required by which the potential gradually changes.

TABLE SHOWING THE RELATION BETWEEN THE VOLTS USED AND THE NUMBER OF MILLIAMPERES of current resulting with various Resistances in Ohms of the Body.

Ohms resistance of the body =	100	300	500	750	1000	1500	2000	2400	3000	4000
No. cells used.	Volts.									
	Milliampères									
1	1½	15	5	3	2	1½	1	¾	5/8	½
2	3	30	10	6	4	3	2	1½	1¼	1
3	4½	45	15	9	6	4½	3	2¼	1¾	1½
4	6	60	20	12	8	6	4	3	2½	2
6	9	90	30	18	12	9	6	4½	3¾	3
8	12	120	40	24	16	12	8	6	5	4
10	15	150	50	30	20	15	10	7½	6¼	5
14	21	—	70	42	28	21	14	10½	8¾	7
16	24	—	80	48	32	24	16	12	10	8
20	30	—	100	60	40	30	20	15	12½	10
24	36	—	120	72	48	36	24	18	15	12
28	42	—	140	84	56	42	28	21	17	14
32	48	—	—	96	64	48	32	24	20	16
40	60	—	—	120	80	60	40	30	25	20
50	75	—	—	150	100	75	50	37	31	25
60	90	—	—	—	120	90	60	45	37	30
67	100	—	—	—	132	100	66	50	41	33

By the above table the Resistance in Ohms of any part of the body, is found by noting how many m.a. are registered with the voltage used.—R Edwards.

Differences between "Electrolysis" and Ionic Medication.

Electrolysis and Ionic Medication must be separated in their therapeutic aspects. In electrolysis the object is to utilise the effect of the ions when they *reach the electrode*; in ionic medication it is the ions which *leave the electrode* that are utilised. In ionic medication the ions pass through the tissues into the protoplasm of the cells.

In electrolysis if astringent and caustic effects are desired the *positive* electrode must be applied. If softening and breaking down

are wanted the electrode applied, at the *negative* pole, must be the active one. In either case the effect is due to the ions of the tissues, not to any extrinsic ions.

In ionic medication on the other hand, it is much more a question of the *chemical to be employed* and the pole to be used is determined by the electric charge on the ions to be utilised.

In electrolysis a non-electrolytically soluble electrode is used such as Platinum or Carbon, in ionic medication the electrode is the substance whose ions it is intended to introduce where this is possible.

—S. Sloan.

A. R. Friel in some 'Notes on Treatment of some Affections of the Nose and Ear,' sums up the differences as follows:—

Ionisation. (a) the introduction into the tissues of ions from a solution of a salt, or (b) the exchange of ions between cells and fluids in the tissues under the action of the constant electrical current. *Electrolysis.* (a) the introduction of ions into tissues from solid metals in contact with their surface, or actually pushed into them, (b) the action on the tissues of chemical substances, e.g., acids or alkalis formed at the point of contact between tissues and metal.—L. i./23, 1305.

For recent discussions on the *raison d'être* of Ionic Medication, see Iodine in this chapter.

In arthritis and sciatica benefit from iontophoresis is more likely due to the interpolar migration of the normal ions of the tissues than to the bodies used locally. The mere passing of the galvanic current will bring from the cathode side of the Calcium Zone the phosphoric acid ion which will dissolve the Calcium precipitated in the tissues—flushing the part affected.—S. Sloan.

Summary of Various Chemicals Employed by Ionisation, with References to their Uses.

The following is a short *résumé* of the Chemicals used and the results obtained by iontophoresis. The medicament is carried through the tissues of the patient who is situate between the two poles. One may regard the human body, from the iontophoresis standpoint, as a solution of sodium chloride, and as the positive ions, i.e., metals, etc., enter from the anode they displace some sodium ions, which emerge under the cathode. Again, as negative ions, e.g., iodine and bromine, penetrate under the cathode, they displace chlorine ions which appear at the anode.

Ieduc pointed out that using simple weak acid solutions the effect on the skin at the anode by the H ion is the same for all ordinary acids. Using dilute alkaline solutions one introduces OH ions at the cathode. In each case the sore produced by a long or strong application has its own characteristics. The K or Na or Mg ions produce definite effects only when given in large amounts. The alkaline earth metals, however, produce characteristic destruction of the tissues. He instances effects obtained when using Calcium Chloride solutions—the surface at the anode seemed white as though impregnated with Calcium Carbonate or Sulphate. Oedema occurred and an indurating ulcer was formed.

Of all ions the most painful was that of Carbonic Acid.

Sulphuric Acid produces a smooth, hard, dry skin surface.

As already outlined, the + ions (basic radicles) in a solution undergoing electrolysis travel from the positive pole towards the negative.

and the - ions (Acid radicles) move away from the - pole. If we imagine the patient separating the solution into two parts with one pole of the battery in each part the - ions will pass into the patient to make for the + pole, and the + ions will be passing from the other side. These new ions displace those already in him (of the same electricity), these in turn displace more, and at his opposite side some of his own ions pass out into solution. The solutions can be different at the poles; one may at one time have Potassium Iodide on the - pole driving in Iodine and Sodium Chloride on the + pole introducing Sodium.

Oily applications must be removed before treatment, as they are non-conductors of electricity.

Pure Water is a non-electrolyte—it contains practically no ions.

A variety of copper chain-mail electrodes are used. Gold or platinum would be better. The latter should in particular be used with organic substances.

Solutions for Ionisation must be made with fresh distilled water. Materials should be washed in the same. The metal of the anode should, if possible, be the same as that of the electrolytic solution.

LIST OF MEDICAMENTS USED BY IONTOPHORESIS.

Acids, whether for introducing the positive (Hydrogen) or the Hydroxyl (negative) ions should be used in 1 in 1,000 solution.—Leduc.

Cauterisation of the glands of the skin can be shown under the anode by the penetration of the H ion.—*cf.* Hydrogen Ions.

Acid Monochloracetic $\frac{1}{2}\%$ with Sodium Chloride 1% used by iontophoresis in gonorrhœa, 2 to 3 *m.a.* for $\frac{1}{2}$ hour. Results successful.—C. Russ, B.M.J. i./17,616.

Alum.—Ionisation with 2% solution useful in relaxation of the tympanum.—L. Kesteven, B.M.J. ii./17,423.

Antiseptics, can be introduced to whatever depth may be required.—Leduc.

Arsenic acts as a vaso-constrictor of the skin vessels. A solution of arsenious acid 1 in 200 introduced on the Kathode every second day for 10 minutes has been used in ionic treatment, *e.g.*, in psoriasis.—B.M.J., ii./12,489.

Bases applied under the Kathode show the cauterisation of glands by the penetration of the OH ion.

Bromine Ions have well marked sedative action.

Butyric Ions have been suggested in lupus.

Chlorine *vide* Sodium Chloride.

Cocaine (from the positive electrode) using a solution of the Hydrochloride 5 to 10% strength—the skin sensibility is abolished in 10 minutes; has given speedy relief of pain in tabes dorsalis. Suitable for minor surgery.

The following solution has also been advised.—Cocaine Hydrochloride $1\frac{1}{2}$ drachms, Solution of Adrenalin (1 in 1,000) 2 drachms, Water *q.s.* to 2 ounces. No toxic effects have been observed. Useful for hæmorrhoids.

The hyperæsthesia and hyperæmia produced may persist for some days, and are succeeded by brown pigmentation. The method is considered bad for local anæsthesia.—N. S. Finzi, B.M.J.ii./12,1180.

In removing moles by epilation Cocaine solution 5% electrolytically for 5 minutes is useful.—Lewis Jones.

Copper Ions employing Copper Sulphate solution have proved effectual in ringworm. A copper electrode connected with the positive terminal has been employed in hæmorrhoids, but according to N. S. Finzi, Copper Ions are deposited entirely in the epidermis, not even reaching the corium.

Trachoma has been treated with Copper Sulphate 0.5% with two to three *m.a.* for two or three minutes every few days. Alopecia areata and lupus erythematosus have been treated.

Rectal cancer treated by copper ions—followed subsequently by zinc ions. Tampon soaked in 2% zinc sulphate inserted and the parts covered with 16 layers of lint. The + pole electrode was attached to the pad and the — to the lumbar region. 60 *m.a.* *ct.* for 30 minutes on alternate days. Good result.—M. Wardle, B.M.J.ii./19,495.

Iodine Ions.—Chronic rheumatoid arthritis, fibrositis and allied joint affections have been treated with Iodine ions using Potassium Iodide or Lithium Iodide solution 2%.

David Campbell (B.M.J.ii./23,409) issued a **condemnation of Ionic Medication** or, at least, a critical examination of the subject. In man, exact records showing that drugs can be utilised in this way are few. He has been unable to confirm the penetration of the Iodine ion, nor has he been able to demonstrate the presence in the body of the Salicylic anion, nor the kations, Pilocarpine and Atropine, after having been carried through the human skin. He shows that pharmacological action of any particular ion is the same whether it be passed through the skin into the body by inunction, hypodermic needle or electric current. Minute amounts only of Iodine, according to the increased amperage, 25 mgr. with 30 *m.a.* and so on, were found in the 24 hours' urine after ionic treatment for 40 minutes, using a 2% Potassium Iodide solution. The total amount of Iodine introduced was only 0.77 grains (for 30 *m.a.*), 1.4 grains (for 50 *m.a.*), 2.46 grains (for 96 *m.a.*), and 3.76 grains (for 200 *m.a.*). 'Local concentration' also was not proven more than a hypodermic injection would give, and there was no evidence of 'deep penetration.' Salicylic Ionisation, likewise, has severe criticism (see also Zinc Ionisation).

C.E. de Silva has a good rejoinder (*ibid.* p. 613). The quantity of Iodine (depending on the **electro-chemical equivalent** of Faraday) introduced into the body is 0.078 mgr. per *m.a.*-minute. In 40 minutes, 9.62 grains of Iodine was **metabolised** in Campbell's 200 *m.a.* instance, and only 146 mgr. excreted in 24 hours. The position of the **Indifferent** pole is **important** for localising effect.

The electric current in living tissues consists of nothing but the *double current of ions*. In the Ionisation of Iodine, *electrons from the generator enter the dissociated Iodine atoms and these ions go through the glands of the skin and the liquids of the body. The atoms travel with their charges, and at the same rate; they are inseparable, even if the ions pass from one liquid to another of different composition (Lodge).* On reaching solid conductors, like muscles, nerves, ligaments, etc., of different density and conductivity, the charges and the Iodine atoms separate, but not before. The electrons get re-embodied in the atoms of the body juices, and there is an **interchange of ions** all along the path of the electrons to the opposite electrode, when again the ions become disembodied and are conducted along the wire. Each act of disembodiment and re-embodiment of the electrons means a modification of the ions and an adjustment of the electric equilibrium of the different tissues, particularly of the diseased tissues. The cells of the body **metabolise the iodine**, the exhausted cells

get re-charged with electricity, germs are killed, toxins neutralised, and healthy function restored. With each treatment, more and more Iodine is unloaded along the path of the ions, and concentration and penetration are gradually increased.

As a further rejoinder, Mark Wardle details his own and other cases. Gouty arthritis well treated; cancer of the tail of the pancreas, the size of a lemon, reduced by Zinc, and so on.—*ibid.* 659.

David Fyfe refers to the results obtained by the late S. Sloan in septic conditions of the uterus and cervix with Copper ions, and his own good results with septic foci about tooth sockets.—*ibid.*

See also C. A. Robinson, *ibid.* 660.

Dental Use of Ionic Medication.—Owen Morphy analyses David Campbell's criticism. The procedure is justifiable in dentistry, *e.g.*, in PYORRHOEA—the small amount of nascent Iodine may be of value. The coagulating power of Zinc ions in root canal therapy tends to promote dryness of the apical region, so difficult of access. Also useful in pyorrhoea.—*L. i.*/26, 823.

Intensive Ionisation (100 to 200 *m.a.*). Report of a Discussion on a paper by W. S. Whitcombe, Roy. Soc. Med., March 16, 1929.

These large doses are needed for dealing with ARTHRITIS of the large joints and deep-seated lesions of the fibrous and nerve tissues in lumbago, sciatica and spinal diseases. Small doses (15 to 30 *m.a.*) thought useless, though, effectual in BELL'S FACIAL PARALYSIS. Discussion as to whether the chemicals, *e.g.*, Cocaine, or the Iodine or Salicylic radical, are actually driven in. A favourite electrolyte with the speaker is a solution of Potassium Iodide and Sodium Salicylate, *a.a.* 2%. 25 minutes is the limit of endurance with most patients. DISSEMINATED SCLEROSIS powerfully influenced. The treatment thought to be curative for all forms of NEURITIS, FIBROSITIS, LUMBAGO and CHRONIC ARTHRITIS, excepting cases of rheumatoid arthritis, in which the disease has progressed so long that the cartilages are destroyed, and the articular ends of the bones are rubbing against one another. In such cases the help of a mechanical support is necessary.

The writer (W.H.M.) examined the solution in a pad after use on a patient by Dr. Whitcombe. It contained 4.98% Potassium Iodide, as against 5.013% in the control solution, or a difference of 0.033%. As 16 ounces of solution were employed, the second figure gives a total of 350.912 grains started with, of which 348.608 grains remained in solution in the pad, a difference of 2.304 grains.

E. P. Cumberbatch expressed surprise at the use of currents of 150 to 200 *m.a.* He considered that density also should be stated. With electrodes 4 inch by 3 inch the density of the current would be 8 or 9 *m.a.* per sq. in., about the highest the skin could stand. He himself had had good results from currents of greater density. Assuming that the Salicylic and Iodine ions reached the affected part, it was too much to assume that they would have any effect, as they were in no sense specifics. Higher saturation could be got by taking these drugs *per os*. The only ions capable of producing effect by electrolytic force were the Zinc ions, and it had yet to be proved that ions other than Zinc could produce therapeutic effects.

C. A. Robinson pointed to an underlying fallacy. The human body is not a simple electrolyte. If real good is to be done in arthritis, one must realise that all these cases are due to some fundamental condition which must be treated. Cases sometimes occur in which almost any type of physical treatment would cure, *e.g.*, Ultra-Violet Light, Radiant Heat, or Ionisation, but in these there is some metabolic or endocrine disturbance which has come to an end, or become altered, or the focus of infection has died out. The importance of local treatment must not be unduly stressed.

Dr. Whitcombe replied. With regard to the question of the density, the electro-positive pad which he used was 63 sq. in., and the negative pad 130 sq. in. The current worked up to that night in the case demonstrated, was 145 *m.a.*, which was maintained for 25 minutes: the negative pad was on the left and the positive pad on the right hip. The patient, before leaving, had told him that he now felt no pain at all. As to the question of the nascent ions, one does not get a nascent ion through the mouth—one gets a solution of Potassium Iodide through the stomach.

Lead.—Grafted tumours treated by ionic medication with a variety of metals, especially Lead.

Borrell, Coulon and Boez found that it was possible to introduce on to the surface of tumours in mice, kations, by ionic medication. A variety of salts were employed at the anode, for example, Lead Nitrate, Copper Sulphate, Silver Nitrate and Barium Chloride. In the case of Lead Nitrate, 10 rats treated gave as result 8 rats cured.—*Comptes Rendus de Séances, Société de Biologie*, Nov. 25, 1922.

Magnesium.—Magnesium ions (from the positive pole) using a Magnesium Sulphate Solution 20 grains to the ounce, have given good effects in multiple warts on the hands. Current 5 to 8 *m.a.*—duration 15 minutes if possible.—Lewis Jones.

Mercury.—Primary syphilis treated by Mercury ions using 2% Mercuric Chloride Solution.—*B.M.J.* i./14,138.

Mercury Oxycyanide.—Pruritus ani well treated by ionisation, using a 1% solution.—*B.M.J.E.* i./27,2.

Mercuric Potassium Iodide.—Mastoid cases can be arrested by ionisation of a solution of Mercuric Potassium Iodide 1 in 500 for periods of $\frac{1}{2}$ hour morning and evening with 5 *m.a.* current.—L. Kesteven, *B.M.J.* ii./17,423.

Quinine Acid Hydrochloride.—Herpes zoster, especially herpes zoster ophthalmicus, has been treated—applications being for 15 to 30 minutes with a current of 1 to 1.5 *m.a.* per sq. inch.

Neuritic and rheumatic pains treated with Quinine Hydrochloride 2% (from + pole), also Sodium Salicylate (from — pole), Potassium Iodide 1% (from — pole), with 2% Sodium Chloride at the indifferent electrode.—W. F. Somerville, *B.M.J.* ii./21,825.

Silicon.—Landry and Franquet claim that the introduction of the ion represented by SiO_3 into the typanum relieves the tinnitus associated with sclerotic changes in the middle ear.—Review, *B.M.J.* ii./28,313.

Silver Ions have been used for infective cystitis and in ulcerative colitis.

GONORRHOEA.—Promising results using Colloidal Silver.—*L.* i./25,449.

Gonococcic subacute or chronic metritis treated. Intensity 20 *m.a.* for 5 or 10 minutes with two seances per week.—A. Zimmern, *Arch. Radiol.*, 1922, 26, 307.

Sodium Chloride.—Resolving influence on sclerotic and cicatricial formations by a kathodal stream (Cl ions), using a slightly warm dilute solution (1 to 2%), applying the cathode to the affected region. The anode may consist of a bath for the feet or arms. Up to 100 *m.a.* 'doses' in several seances. Rheumatic sclerotitis and perisclerotitis are stated to yield well.

For data showing the No. of *m.a.* obtained on passing a current of 50 volts through various salt concentrations, see *Edn. XVIII.*, Vol. II., p. 276.

Scars, painful, of the face, treated by Cl. Ions—better for softening scars than iodides or salicylate.—H. S. Carter and A. D. E. Shefford, *B.M.J.* i./19,214.

Sodium.—Superfluous hairs, nævi, etc., are removed by electrolysis the saline solution of the body, *i.e.*, by producing Caustic Soda at the—pole.

Sodium Salicylate.—For painful pleurisies and intercostal neu-

ralgia, 2% solutions. Tic douloureux of the face, sciatica, and infective cystitis have been treated.

Corns yield to Salicylic ions.

In sciatica successes not brilliant. Possibly for the last mentioned powerful treatment (200 *m.a.* applied for 1½ hours) necessary.—Lewis Jones.

Acute articular rheumatism. Cases of benefit have been recorded—see also Recent Discussion under Iodine.

Furunculosis of the external auditory meatus, Ionisation with 2% Sodium Salicylate solution is the best treatment.—per Pr., Apl., '27,270.

Strychnine.—Toxic effects can be produced. Note the ions in this case diffuse rapidly, sufficient to produce death in a few minutes.

Zinc Ions.—Antiseptic of the first rank. There is no wound which cannot be disinfected by its use.—Leduc.

GROWTH OF HAIR is stimulated by Zinc Ions in feeble doses Stronger doses may produce death of the tissue.

MENORRHAGIA.—60—100 *m.a.* with the Zinc Anode for 20—30 minutes. The Zinc is not absorbed. A good coagulating medium.

ENDOMETRITIS has been treated with a uterine Zinc Anode, infective cystitis also and old-standing ozæna.

RODENT ULCER.—The Zinc electrode is wrapped in lint soaked in 2% Zinc Chloride Solution. It is attached to the + end of the battery and the negative electrode is soaked in Saturated Salt Solution—applied to nape of the neck—within limits it should be as large as possible. Current 2 to 3 *m.a.* for each sq. cm. of surface. A reaction ensues and subsides and healing may be effected in 10 to 14 days. A second application may be given fourteen days later. Cocaine may be ionised into the part beforehand if desired.

A 4% solution of zinc sulphate may be used instead. The electrodes should not be touched with the fingers, as sodium chloride and other impurities may be introduced. The application is continued for ten to fifteen minutes, according to the thickness of the ulcer. Patients can bear up to ten *m.a.* without complaining. The Zinc Ions seem to remain in the cells of the part for some time. The rate of movement of the ions in such a case is probably less than 1 cm. in 1 hour, the amount of zinc set in movement in an ordinary application of 10 *m.a.* for 10 minutes is about 4 mgr.—Lewis Jones.

Lupus vulgaris, lupus erythematosus and epithelioma. Chronic pharyngitis, ozæna, pustular eczema and hypertrophic rhinitis, chronic urethral catarrh, also diphtheritic infections of the skin, warts and lupus have been treated.

Otorrhœa treated. 3 *m.a.* periods of 5 to 15 minutes.—A. R. Friel, L. ii./20, 345. Distinctly more rapid in effect than other methods. 68 out of 78 cases remedied and remained dry for 6 months.—J. A. Keen, Pr., July, '28,43.

Corneal ulcers have been treated by ½% solution with current 2 to 4 *m.a.* for ½ to 1 minute. First "cocainise." In obstinate blepharitis 3 to 5 *m.a.* for 3 to 5 minutes.

For a case of simple cervicitis the zinc or copper electrode, covered with cotton wool, is inserted into the cavity of the cervix through a speculum which is filled with a 1% solution of Zinc (or Cupric) Chloride.—S. Sloan.

GONORRHOEA.—Ionisation gives good results. Maringe's method described The current used is from 15 to 20 milliamperes, this is passed for from 5 to 10 minutes from mercury bisulphate batteries. The positive current is used first then reversed a few moments and stopped. The application is made every five days.—Pr. Oct., '10,420.

COLITIS treated by making the + pole a rectal electrode to which is attached a 2 pint douche of Zinc Sulphate Solution 2% (warm), about ½ pint of this is run in and the current gradually turned on to 15 or 20 *m.a.* The current is allowed to pass to a negative electrode which is a combined dorsal and lumbar one for 15 to 20 minutes. The Zinc ions in this way pass thoroughly through the diseased membrane to the — pole. Gratifying results.—L. i./11,1068, B.M.J. ii./12,486. cf. Silver.

LUPUS VULGARIS.—2% Zinc Chloride solution or a 10% solution of Zinc Sulphate is applied, using a Zinc electrode attached to the positive pole. 2 to 3 *m.a.* for each square centimetre of surface is a suitable intensity—for 10 to 20 minutes. Apply a Calamine or Lead Lotion to the crust which forms later. The treatment may be repeated every fortnight.

CHRONIC ULCERS AND SINUSES.—Zinc—in cases of chronic mastitis and chronic cystitis, using a Zinc rectal electrode, has given good results. In dermatology, wipe over the nodules with Caustic Potash Solution to dissolve off the gelatinous covering, then wash with saline solution or distilled water, and expose for twenty minutes to Zinc ionisation. Repeat if necessary after 14 days.

Bedsore ulceration, rectal ulceration, hæmorrhoids, anal fissure, ulceration in the mouth and nose, sinuses (chronic suppuration of the antrum), urethritis, vaginitis and leucorrhœa, skin affections (acne, furuncle, ringworm), well treated.—Lewis Jones, B.M.J. i./11,887; ii./12,486; ii./13,938.

SUPPURATION in maxillary, frontal and sphenoidal sinus treated with Zinc ionisation. Solution used, Zinc Sulphate 75 grains, Glycerin 2 oz., Water to 70 oz. Current 10 to 15 *m.a.* for $\frac{1}{2}$ hour.—A.R. Friel, B.M.J. ii./21,404.

Chronic suppuration of middle ear treated by ionisation of solution of Zinc Sulphate 5, Glycerin 57, Water to 1000.—A. G. Wells, L. ii./21,1268.

Value of Zinc ionisation in all septic ear and nose affections.—A. R. Friel, B.M.J. ii./22,42; L. i./23,1305.

SUPPURATIVE OTITIS MEDIA responded. The ear is thoroughly cleaned by syringing twice daily for a week with a solution containing equal parts of Potassium and Sodium Chloride, Sodium Bicarbonate and Borax. After syringing with sterile water and anæsthetising with Cocaine, the tympanic cavity is filled with Zinc Sulphate solution 2%, a Zinc electrode placed in the meatus and connected with the + pole, and the — electrode placed on the leg over a pad of lint soaked in saline. A continuous current, gradually increased to 3 *m.a.* is passed and controlled by a rheostat for 10 to 15 minutes. The current is then gradually decreased to zero and the ear carefully dried and a little Boric Acid Powder insufflated.—W. E. Crosbie, B.M.J. i./27,918. See also T. B. Jobson, B.M.J. i./24,371.

D. Campbell (B.M.J. ii./23,409) gives a good criticism of Zinc ionisation as practised. A number of Electro-therapeutists use simply a Zinc probe which is inserted into a sinus, or a Zinc sound which is passed into the uterus, the metal forming in each case the + electrode. Destructive action follows when the current is turned on. The Chlorine ions of the tissues move to the Zinc electrode, give up their electrical charges, and the Chlorine atoms thus set free combine with the Zinc, making nascent Zinc Chloride with caustic and anti-septic effect. But *that is not ionic medication*. It is simply making Zinc Chloride where its action may be of value. A similar state of things occurs, no doubt, when the Zinc rod is in the cavity containing a solution of Zinc Sulphate, for there will be constantly produced electrolytically nascent Zinc Sulphate by the Sulphuric ions giving up their charges at the Zinc electrodes, and the atoms thus formed combining with it. *See also under Iodine.*

Zinc Iodide.—Middle ear catarrh treated by ionisation of 30% Zinc Iodide solution with 3 to 4 *m.a.* of current. Goitre has yielded to ionisation with 5% Zinc Iodide as also acute tonsillitis and enlarged prostates and enlargement of the turbinates.—L. Kesteven, B.M.J. ii./17,423.

Dental Application.—The maximum current employed is usually about 5 *m.a.*

PYORRHŒA ALVEOLARIS is well treated by 2% Zinc Sulphate applied at positive pole for 10 to 15 minutes with a current of 2 to 4 *m.a.*

For chronic alveolar abscess 2% Zinc Chloride or Copper Sulphate Solution with 3 to 5 *m.a.* 5 to 10 minutes. The sinus can be easily treated by means of Copper or Zinc wire 0.3 to 0.5 mm. thick.

Ionic medication should be employed in all cases of pyorrhœa alveolaris. A variety of astringent solutions can be used in this way.—G. B. Pritchard, L. i./27,92.

PERIODONTITIS.—2% Zinc Chloride with 2 to 4 *m.a.*

In many forms of gingivitis and chronic alveolar abscesses effective.—cf E. Sturridge, B.M.J. ii./12,487,491.

Eye Work. The electrolytic solutions must be dissociated as much as possible— $\frac{1}{2}$ to 2% solutions suitable. The "electrode cushion" must be of uniform thickness, and so thick that the ions where it comes into contact with the metal plate cannot penetrate into the tissues during application. It is important to realise that the lachrymal fluid is an electrolyte on account of the Sodium Chloride contained. Further there is the influence of the Cocaine used as anæsthetic. Cocaine kations are very active on the cornea. Special electrodes and mode of treatment of the conjunctiva, edges of the lids and cornea are described.—Oph., Jan., 1911, p. 18. See also references under Sodium Chloride and under Zinc.

"Solubes, Ionic," for Medication, are prepared of many of the above substances. Each represents 4.375 grains (0.28 Gm.) to produce a 1% Solution on dissolving in 1 ounce of water. Two in an ounce make 2% solution, and so on within limits of solubility. The following are examples:—

[P] Cocaine Hydrochloride.	Potassium Iodide.
Lithium Sulphate.	Quinine Acid Hydrochloride.
Magnesium Sulphate.	Sodium Chloride.
Zinc Sulphate.	

'Sterules,' Ionic, of many solutions are also made.

References.

For a theoretical study consult 'Conveyance of Electricity through Solids, Liquids, and Gases and Production of Radiation.'—Sir Oliver J. Lodge, B.M.J. ii./11,885. For gynæcology.—S. Sloan, L. ii./11,1759; B.M.J. ii./12,491.

FRESH AIR v. VITIATED AIR. Expired air is destitute of ions. If the ionic content of air has a benignant effect on human well-being, its treatment in modern systems of ventilation (passing through water) deprives it completely of this energy content. The so-called 'fresh air' of these artificial systems of ventilation is 'dead.' Ionic differences, both physical and physiological, between fresh and vitiated air should be further investigated.—J. P. Kinloch, B.M.J. ii./22,357.

RADIOLOGY.

"X" Rays, discovered by Roentgen* in 1895, are produced in a vacuum tube on the passage of an electrical discharge of high tension from a Ruhmkorff coil†, at the point where the cathode rays (electrified particles emitted at a high velocity normally to the surface of the cathode) strike solid matter. In the old form of "X" ray tube this was the glass of the tube itself; in the new form (the invention of Jackson and others) the anti-cathode, which is also the anode and is usually of tungsten, receives the rays from a concave cathode, which is of aluminium. They are focussed by its concave surface, and the "X" rays (ether vibrations or pulses) are propagated from the *front* of the tungsten plate (which is set at an angle of 45° to the axis of the tube) in all directions into space at the velocity of light. For a more

*Roentgen's original paper is reproduced (in English) in the J.R.S. of July 1923.

† A Coil termed the *Sunic Rectipulse Coil*, Patent 7311/15, produces high tension impulses entirely unidirectional and dispensing with valve tubes on coils. The apparatus provides current in which the secondary impulse due to the make in the primary current does not oppose that impulse due to the break, but appears in the same direction. This effect is produced by the arrangement of the primary current in such a way that the magnetisation of the iron core is reversed in sign at each successive impulse.

recent view of the relation between "X" rays and cathode rays, *cf.* Radium—"γ" rays.

In working from electric supply mains if current is not continuous, a high tension transformer is necessary, *e.g.*, that of Gaiffe or Koch.

In Coolidge's Tube the anode consists of heavy tungsten, while the cathode is a spiral of tungsten wire, heated by a low-tension circuit. There is no fluorescence. Streams of charged particles from the tungsten cathode are driven by a powerful high-tension current against the anode, and the rays are formed; these are more or less penetrating in proportion to the speed with which the particles are driven, hence intensity can be controlled by varying the voltage of the high-tension circuit.

A useful account of the various advances in Coolidge Tubes.—Maj. G. W. C. Kaye, Jl. Rontg. Soc., Apl., '20.

In Germany, Coolidge tubes are employed which are claimed to stand up to 300 kilowatts, but the patents preclude the use of these in this country.—N. S. Finzi, B.J.R., Apl., '25, 68.

The largest commercial Coolidge tube operates at 250,000 volts, and 50 *m.a.* with continuous output. The anode is water cooled and the glass bulb 8 ins. in diameter. The smallest tube operates at 56,000 volts (max.) and 10 *m.a.* is mounted in oil, and has a glass bulb 1½ ins. in diameter—this is used as a portable X-ray outfit.—B.J.R., Apl., '25, 82.

'Gas Tubes' have improved. They act more regularly by means of a special arrangement serving to give a part of the glass of the bulb the full positive charge. In Philip's Bulb the strong metal parts and heavy anti-cathode block render the tube suitable for rapid radiography. An improvement is in doing away with the third anode, and silvering the glass behind the anti-cathode instead. This adds considerably to the steadiness of running.

Gas Tubes give best results.—Discussion Soc. Radiog.—B.J.R. June, '28, 210-217.

Metallix tube (Patented throughout the world). A relatively small current can be used. It embodies its own device for protecting the operator, the wall being practically impervious to the rays, and only those which are used are passed out. The cylindrical shape is convenient. Made with exceedingly fine focus for radiography and broad focus for treatment.—L. li./24, 562.

The "X" Rays resemble light rays in almost every particular, the chief difference being that the X-Rays have wave lengths about 5,000 times shorter, *i.e.*, the X-Rays are situated far beyond the violet end of the visible spectrum, and may be regarded in a sense as a 'treble' form of ultra-violet light. This very minuteness of wave-length—a distance of the same order as the size of atoms—defeated all the earliest attempts to direct and sort out the rays. Just about a single octave of light waves is visible to the eye.—R. Knox, B.M.J. i./22, 631.

"X" rays possess the power of exciting phosphorescence and fluorescence.

Many substances are almost transparent to the rays, *e.g.*, paper, leather, wood, soda-glass, mica, sulphur, indiarubber, cotton, wool and silk. Others, like bone and glass containing heavy metals, *e.g.*, lead, are semi-opaque. The metals are opaque in approximate proportion to their atomic weights—lead and platinum being almost entirely opaque, whilst aluminium is comparatively transparent. Iodine and Iodoform are very opaque.

Barium Platinocyanide Screens are fluorescent to the rays and render the shadows of the opaque bodies visible. They are made by coating cardboard or other suitable material with a film of Barium Platinocyanide suspended in a solution of Celluloid in Amyl Acetate.

Screens are now made with substances other than Platinocyanide. Their brilliance of a screen depends to a great extent on the molecular weight of the fluorescent compound.

The **SUNIC WHITE SALT SCREEN** made with **Cadmium Tungstate** gives good contrast and definition and is unaffected by continued use. Other manufacturers employ **Willemite**. The advantage of the Cadmium compound is that when properly treated there is practically no after-fluorescence.

For a recent account of Screens, see L. A. Levy and D. W. West, B.J.R., July, '25, 104-118.

"X" ray tubes are called "**hard**" *i.e.*, those with high penetrative power in which the resistance is great—and "**soft**," *i.e.*, with only slight penetrative power, hence producing a dull radiograph as the rays from it are stopped to the same extent both by flesh and bone. These differences are principally due to the different exhaustion of the tube, a very high exhaustion producing the hard effect, and only one of partial extent gives the soft or dull results, but the size of the electrode also affects the results, *e.g.*, a small cathode gives a high resistance and high penetration, and a large one the opposite effects. The decisive factor is the voltage of the high-tension current. The greater the resistance imposed by the tube, the higher the voltage rises (within limits imposed by the capacity of the apparatus) and the greater becomes the penetration of the X-rays generated. Best contrasts are obtained with a tube of medium softness.

Tubes are now made so that they can be regulated to any degree of softness, and are also automatically self-regulating, so that when the resistance becomes too great, an alternative spark gap comes into play which liberates gaseous matter and thereby softens the tube.

In bi-anodal tubes an additional electrode of aluminium is fitted behind and to one side of the anti-cathode and is connected with it outside the tube by a piece of wire; this permits the passage of much heavier discharges, and the tube works "**steadier**." The glass of the tube is of soda glass, but special bulbs, in which lead-glass is employed, with the exception of a window which is of soda-glass, are used for the application of the rays in skin affections. These obviate the necessity of shielding the normal tissue from the action of the rays. Special shapes are also made for the application of the rays to various parts of the body, *e.g.*, by introduction into the uterus.

The value of a tube depends on its solid construction and the definition of the radiograph produced at a distance of a foot. Exposures necessary with good photographic plates (special rapid plates are made for "X" ray work) have to be ascertained for the particular tube employed. It is stated that for the foot and ankle the exposure should be three times that necessary for the hand and for the trunk ten times. The arms and legs below the knee require about four times that for the hand; the abdomen may require thirty times that necessary for the hand.

Tubes made with **Borate of Lithium** and **Beryllium**, *i.e.*, low atomic weight elements, *viz.*, with weights 11, 7 and 9 respectively, absorb only 1/5 of the amount of "X" rays of medium hardness absorbed by ordinary glass. Erythema may be produced by using tubes of this kind, *e.g.*, in skiagraphy of the chest. The exposure in such examinations using these tubes may be reduced to a third or fourth.

"**Duplited**" Films are more rapid than ordinary plates. Radiographs can be obtained with them by single flash exposures when two intensifying screens are used, thus making for clearly defined images, *e.g.*, of internal

organs. The feature of these films is that the emulsion is coated on both sides of the film so that when an exposure is made, one has the effect of two sensitised surfaces separated by a thin layer of celluloid. They have the obvious advantage of lightness and small bulk as compared with plates.

"X"-ray plates have now almost disappeared. A lecture on the method of manufacture of "X"-ray films.—T. Baker, B.J.R., '28, 330.

Radio-Print Paper for direct "X" Ray photographs on paper has the advantage of eliminating risk of breakage.—G. B. Batten, J.R.S., Jan., 1919.

A new type of plate which reduces radiographic exposures to 1/25 of the normal amount consists of an X-Ray plate with the fluorescent coating of Calcium Tungstate, in a suitable medium, on the sensitive film. This renders it possible to take a number of radiographs without the risk of burns or undesirable results, and reduces the wear upon apparatus, especially tubes.—D. West, T. Bauer and L. Levy, J.R.S., '21, 58 and 104.

Colour-Sensitive Plates.—A type of the Schumann Plate to explore the extreme ultra-violet region of the spectrum by means of vacuum-spectrometers. Details *re* Ethyl-Violet 6B and Isocyanine and Ethyl Cyanine in connection with.—Jl. Rontg. Soc., Jan., 1920, p. 2.

Direct stereoscopic X-ray examination apparatus.—B.J.R., Feb., '29, 73.

Hitherto it has been possible to take "X"-ray photographs only of natural size, and for **cinematography** large numbers of such full-size skiagrams have had to be taken and subsequently reduced—a costly and difficult process. A discovery of Dr. Gottheiner of Berlin reduces the cost of such films by 99%. The basis of the invention is a method for the conversion of "X"-rays into simple light rays of many thousand times longer wave length. The effect is produced by a special fluorescent screen, the image of which is reduced and received directly into a cinematograph film of ordinary size. The development of this discovery presents many important and interesting possibilities.—A. Salmony, B.J.R., Sept., '28, 327.

Silhouette-Radiograph : for bringing out the flesh contour in radiograms. Place the negative in an illuminator and scratch the fleshy contour with a mounted needle; the print will indicate the contour of the limb as a black line. After drying, black in the background with India ink, and when dry squeeze print in the usual way. The picture gives an almost stereoscopic effect, the jet black showing up the bones to great advantage.—A. P. Bertwistle, B.J.R. Feb., '28, 66.

Bismuth Carbonate or **Oxychloride** suspended in Mucilage (1 drachm in the ounce) is used for examining œsophagus and stomach. See Vol. I. pp. 228, 232, 234. It is also used for pathological work, *e.g.*, to inject veins,—to outline them prior to radiographing.

Barium Meals.

The following are palatable mixtures :—

No. 1. *Thick, flavoured, for œsophageal cases* : Barium Sulphate 10 oz.; Saccharin 2 grains; Vanillin 5 grains; Gum Tragacanth 100 grains; Distilled Water to 20 oz.

No. 2. *Thin, flavoured, for gastric cases* :—Barium Sulphate 10 oz.; Saccharin 2 grains; Vanillin 5 grains; Gum Tragacanth 60 grains; Distilled Water to 20 oz.

No. 3. *Thin, unflavoured, for opaque enemata* :—Barium Sulphate 10 oz.; Gum Tragacanth 60 grains; Distilled Water to 20 oz.

The Gum and Barium Sulphate should be mixed as powder, and the water added gradually and then sterilised. This cream shows a very dense and homogeneous shadow.

About 3 to 4 ounces given at first and a further 6 ounces if needed, or if whole of intestinal tract is to be examined.—S. Gilbert Scott, Arch. Radiol. 27, 304. See also Vol. I., p. 222.

Diaphanite.—A mixture of magnetic iron ore, milk sugar and cocoa. A black powder also used as a substitute for Bismuth.

It is important to work with the tube completely enclosed excepting for a small aperture, so as to prevent blurring effect from secondary radiation from the glass of the tube.

Catheters or **Bougies** impregnated with Bismuth are employed in diagnosis of urinary diseases.

Secondary Radiation.

The hard Röntgen rays are little absorbed,—they can pass through the body without suffering any very enormous diminution, hence produce little physiological effect. The soft rays are absorbed more easily than the Beta rays of Radium. The whole of their energy is taken in by a very thin layer of the flesh which thereby becomes exposed to a most vigorous physical agency. It is important to get rid of these soft rays when using Röntgen Rays in exploration,—on the other hand, for treatment of superficial lesions very soft rays are required. Their production is a matter of great difficulty; the best rays are absorbed on their way out of the tube, even if aluminium windows be used,—any kind of window would have to be thick enough to stand the external pressure. A discovery in this direction is of importance. It is well known that when Röntgen Rays strike against metal, or indeed anything, secondary rays are emitted, and their kind depends on the nature of the substance struck. The degree of hardness of the incident ray does not matter,—the quality of the ray given off is constant. One important point is to be remembered, *i.e.*, that in order to enable the metal to give out its particular ray the incident radiation must be harder than the radiation characteristic of the body, *i.e.* a very soft radiation will not excite radiation from a metal of high atomic weight. Rays of almost any degree of hardness or softness may be obtained with absolute certainty by taking advantage of the fact that *the secondary radiation occurring when a Röntgen Output impinges on a metal, varies in hardness precisely with the atomic weight of the metal.*

Metals of lower atomic weight than Calcium do not give out any secondary radiation,—they simply scatter the incident ray, but iron, copper, zinc, silver, etc., have their characteristic radiation. The radiation from iron would be absorbed by 1/100 m.m. of human flesh; those from copper would fall a little deeper. Those from silver have about the same penetration as the β -rays of Radium. Sir J. J. Thomson's suggestion was, therefore, to **expose silver to an "X" ray tube, and utilise the secondary radiation from this element.** Another point of interest is that the energy absorbed by Hydrogen differs from that absorbed by other substances—it depends on the quality of the ray. With the very soft rays given out by iron there is practically no absorption by hydrogen, but as the hardness of the ray is increased the proportion of energy absorbed by Hydrogen increases also. Diseased tissue may differ in chemical combination from healthy tissue, and in one case we may get a larger relative absorption than in another. A ray may be obtained which would be greedily absorbed by the tissues we wish to affect, and not absorbed to anything like the same extent by the normal substance. This may have important bearing therapeutically. See also *Argentum Purum* *Præcip.* p. 34.

Secondary radiation from **Calcium Phosphate** in bone material possibly the means of cure of cancer by Radium. Suggestion to embed a piece of bone material in a cancer and expose to "X" rays from a tube with Uranium Anticathode. The results should be more favourable than those obtained from Radium.—L. ii./13,1804.

Induced fluorescence as an aid to radio-therapy. **Calcium Tungstate** injected plus "X" ray exposures stated to retard growth of experimental tuberculosis.—P.J. ii./13,913.

Silicon Carbide— $\text{SiC.}=40\cdot105$ *Syn. Carborundum*—An exceedingly hard iridescent black crystalline substance made by fusion of Carbon, Sand and Sodium Chloride in an electric furnace. Employed technically in polishing. Used as Anticathode.

The dust of Silica, Graphite and Carborundum Works responsible for lung disease.—E. M. Collis, Int. Cong. Med., 1913; B.M.J. ii./13,406.

"X" Ray Shields.—Iron and Copper should be avoided in making shields—they give out all the soft rays by secondary radiation. Metals with higher atomic weights give more penetrating secondary radiation and hence go through the flesh with less absorption and so produce less evil effect.—Sir J. J. Thomson, *cf.*, above.

Red Lead and Plaster of Paris casts to enclose the "X" ray tube, also thick **Lead Glass Frames** over the fluorescent screen are necessary safeguards. **Leaded Rubber** is also used for shielding purposes.

Glass Shields containing a high percentage of lead, are employed with a window opposite the anode through which the rays pass, and have the advantage that the tube can be watched.

The operator should at all times stand behind the plane of the anode.

Ionized air is injurious if breathed continuously; a large well-ventilated room should be employed.

Silk impregnated with metals arrests "X" rays, *e.g.*, silk treated with lead phosphotannate and other salts containing 68% of mineral matter, including 34% lead oxide, 24% Tin Oxide, 8% Phosphoric Anhydride and 2% of Lime and Alkalis. Slight discharges of "X" rays were practically arrested by this while 6 layers were sufficient to protect the skin against ordinary discharges of medium strength. As effective as Sheet of Copper 0.044 mm. thick.—M. L. Droit, Knowledge, Feb., '13, per P.J. i./13,164.

Protection in Diagnostic work. Methods employed against scattered rays and secondary rays.—F. Hernaman-Johnson, Jl. Rontg. Soc., Apl. 19, p. 45: see also R. Knox, Jl. Rontg. Soc., Jan. 1920, p. 17.

BLOOD-COUNTS to indicate efficiency of X-Ray and Radium protection.—J. C. Mottram, B.M.J. ii./21,269. Some are sceptical of accuracy of the method and conclusions to be drawn.

The subject of *shields*, etc., is fully dealt with under the Protection Committee's Report *postea*.

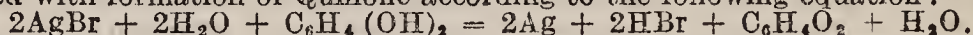
DEVELOPER FOR PLATES (Thomas's):—

No. 1.—Hydroquinone 160 grains, Sodium Sulphite 2 ounces, Citric Acid 60 grains, Potassium Bromide 40 grains, Distilled Water: to 20 ounces.

No. 2.—Sodium Hydrate 160 grains, Water to 20 ounces.

Equal quantities of the solutions are used. It does not stain the hands. Some employ the soda solution diluted so as to develop slowly, and thus produce better definition, but for routine work this takes too long.

In using Hydroquinone as developer, it is believed that the Silver salt is reduced with formation of Quinone according to the following equation:—



It is suggested that in alkaline solution the Hydroquinone combines with water, liberating Hydrogen, which reduces the Silver Bromide. A developer "Borinol" has been elaborated, in which this capacity to decompose water has been reduced, with the result that it exerts a slower but more uniform action on the emulsion.—C.D., '23,904.

Metol-Hydrokinone Developer. The following is representative of solutions commonly in use now.—Metol* 14 grains, Hydroquinone 60 grains, Sodium Sulphite (cryst.) 400 grains, Sodium Carbonate (cryst.) 800 grains, Potassium Bromide 4 grains, Water to 20 ounces. At 65° F. this takes 6 minutes to develop a film. For a solution requiring 18 minutes increase the Sodium Sulphite to 1,200 grains and decrease the Sodium Carbonate to 400 grains.—L. T. Branch, B.J.R., Apl., '28,141.

"X" Ray Diagnosis.—As an aid to diagnosis, "X" rays are now in universal use, *e.g.*, in examining fractures, in diagnosing phthisis, pneumothorax, lesions of the alimentary tract, pleurisy, tubercle, aneurism, enlarged bronchial glands and for the detection

* Note.—Metol is the sulphate of Methyl-*p*-amidophenol $\text{C}_6\text{H}_4\cdot\text{OH}(\text{NH}\cdot\text{CH}_3)$, *i.e.* $[\text{C}_6\text{H}_4\cdot\text{OH}(\text{NH}\cdot\text{CH}_3)]_2\text{H}_2\text{SO}_4 = 344\cdot246$.

The Trade Mark "Metol" (222,338) registered in 1899 has been **avoided**. Patent 15,434/1891 expired 1905.

* **Motlenol** is a trade variety of it. T.M. 349,103.

* **Am dol.** This developer is the hydrochloride of Diamidophenol $\text{C}_6\text{H}_3\text{OH}(\text{NH}_2)_2\cdot 2\text{HCl} = 197\cdot010$.

A German Company registered (No. 234,719) in 1901 a label containing the words "Amidol-Hauff." No. 373025 applies to the substance made in England. No. 363479 is Amidol-Johnson's.

Patents: No. 4498 of 1892 was in force for the whole 14 years. Patent 60,174 (27/1/91) granted to J. Hauff of Feuerbach deals with the use of *p*-Amidophenol and *p*-Amido-cresol as developers, but not with the manufacture of di-amidophenol. For manufacture see C.D. Sept. 19/14, p. 38.

(Para-amidophenol $\text{C}_6\text{H}_4\text{NH}_2\text{OH}$, *Syn. Rodinal*, is made from *p*-nitrophenol by reduction, *e.g.* with iron and acetic acid. M.Pt. 170°).

of renal and ureteric calculi. Tubercular deposits can be demonstrated which have not been detected by ordinary means. In dental surgery the rays are exceedingly useful.

'Cross Thread Localiser'—The late Sir J. Mackenzie Davidson devised an apparatus for measurement and localisation of foreign bodies. Two exposures are made on the same plate, the tube being moved right and left of a zero point on a scale, without the patient moving. On developing the plate two shadows of the foreign body are seen. From these, measurements are taken by means of threads with a surface gauge; this gives the exact depth of the foreign body below the skin. Some prefer to work with two photographic plates instead of one as mentioned. This method is also employed for the measurements of bones, displacements, and especially for pelvic measurements. Is also useful for detection, localisation and estimation of the size of foreign bodies in the eyeball and orbit. A piece of metal, less than a millimetre in diameter, can be detected in the eye. The removal of pieces of steel can be effected by means of the electromagnet.

The **stereoscope** applied to skiagraphs gives the object in relief and shows the true relation of the parts. The skiagraphs are taken from different points of view after displacing the tube about 6 centimetres. By practice it is possible to combine stereoscopic pictures without the employment of a stereoscope.

Description of the method, including the *Telephone* for affixing to surgeons' instruments.—B.M.J.i./15,1 *et seq.*; N. E. Aldridge, B.M.J. i./15,70 and W. Cotton Pr. 1915; *see also* L. ii./16,608; L. i./17,719.

Interpretation of Negatives.

The negative should be examined, as it is more reliable than a print. Cartilage casts no greater shadow than muscle. Calcified cartilage (as in the rib cartilages of old patients) also calcified arteries throw a distinct shadow. Dislocations are usually evident on a skiagraph, but some joints require stereoscopic views. Tumours cast little or no shadow.

Diagnosis of Renal Calculus by means of a Screen.

Once a stone has been seen on a plate there is a strong probability that it can be seen on the fluorescent screen, provided that the patient is not too fat, and that plenty of fluorescence can be seen on the screen. A diaphragm is to be used to stop off all "X" rays except over an area half the size of the kidney. The stone can be seen more distinctly when located by making the patient breathe deeply, and then the stone and the kidney will be seen to rise and fall at least $1\frac{1}{2}$ inches. *A calculus of Calcium Oxalate casts the darkest shadow.* Cystine stones come next in density, followed by Calcium Phosphate. Mixed phosphate stones cast still less shadow, and last in order come Uric Acid stones which may cast no shadow at all. Methods of procedure for diagnosis of ureteric calculi are also given.—A. H. Pirie, B.M.J.ii./10,584,586.

Urinary Tract Examination—B.M.A. DISCUSSION. The apparatus should be capable of making correct exposure in a fraction of a second, or, at most, in 2 or 3 seconds. The tube should be soft rather than hard, with just enough penetration to get through the parts. The entire urinary tract of both sides should be X-rayed in all cases. Unscreened films are preferred, but there is no objection to films of the first quality—they must be free from the slightest markings or grainings. The kidney films should show the whole outline clearly. The mid ureters are next examined. The ureters, or at any rate the greater part of them, do not move with respiration; a shadow, therefore, such as a calcified mesenteric gland, would cast a blur with respiratory movement. Next, the bladder region is examined. The tube must be well tilted, so that with the patient supine the opening of the extension tube points well into the opening of the pelvis. The Potter-Bucky diaphragm is of much value, as is also radioscopy of the urinary tract. With regard to more special methods, perirenal injection of Oxygen or Carbon Dioxide is of value in stout patients in showing kidney stones. Pneumo-peritoneum (injection of Oxygen through a needle into the peritoneal cavity under local anæsthetic) of value, but not without danger. Colon inflation simpler and good when there is difficulty of showing up kidney outline. **Pyelography** is a valuable aid—10 to 20% **Sodium Iodide** or **Bromide** is most in favour. Collargol irritating.

Ideal solution not yet found. Only one side should be done at a time. The special value of pyelography is in outlining the renal pelvis and showing if it is dilated or distorted. It also shows relation of the kidney pelvis to the shadow of a stone in the kidney region. In Cystography, a 10% **Sodium Iodide** or **Emulsion of Barium** (Sulphate) **and Oil** is used. It is well known that a Uric Acid stone casts no shadow; all others cast a definite one. The more rare Cystin and Xanthin stones cast a definite shadow, due to their Sulphur content.—R. W. A. Salmond.

Peri-renal and intra-peritoneal (for urinary tract) injections have, we think been entirely abandoned since this discussion. They have fallen out of favour.

PYELOGRAPHY.—Sodium Bromide 20% Solution for the kidney and 10% for bladder. Casts very distinct shadow but may be irritating. 10% suspension of Colloidal Silver (Collosol) better.—F. Kidd, B.M.J. i./22,748.

Sodium Iodide, 20% solution, as pyelographic medium, casts a deep shadow and is non-irritant.—Lowsley and Muller, JI. Urology, '23,9,1, Y.B.P., '23,61.

Sodium Iodide in 13½% solution best medium. Causes no inconvenience to patient and is easily sterilised.—R. J. Willan, B.M.J. i./26,409.

A 12% solution the medium of choice, but is not germicidal. A dilution of 1 in 3,000 Mercuric Iodide in 12% Sodium Iodide has Phenol Coefficient of 0.033, i.e., equal to 3 to 4% Phenol, and is not irritating.—Jl.A.M.A. i./26,581.

Sodium Iodide solution (100 Gm. in 100 Cc.) injected intra-arterially valuable as X-Ray medium in determining the amount and extent of occlusion of arteries of extremities.—Pres. July 24,286.

Thorium-Sodium Citrate Solution as Pyelographic Medium.

The solutions used a few years ago contain the equivalent of 10 per cent. and 15 per cent. Thorium Nitrate.

For details of manufacture and procedure, see Edn. XVIII, Vol. II., p. 295.

Gall Bladder Examination, see Vol. I., p. 681.

The Normal and Pathological Stomach as seen by "X" Rays.

A radiograph is a record of the picture at one given moment only. Cinematographic radiographs would be more useful than screen work. The aspect of the stomach in cases of atony of the stomach; "dilatation," pyloric obstruction, spasmodic conditions and gastric ulcer hour-glass stomach, carcinoma of the stomach, aërophagy and duodenal ulcer are dealt with.—B.M.J. ii./10,537; i./12,225.

Fallacies with Bismuth.—A. F. Herz, B.M.J. ii./12,775.

Illustrations show a variety of obstructions, e.g., due to malignant growths and aneurism.—Jordan, P.R.S.M., Electro Therapy Sec., Dec. '10, p. 13. See also B.M.J. ii./11,699.

THORACIC ANEURISM.—The only form which is not revealed with certainty by either anterior or oblique examination is a small aneurism confined to the concavity of the arch. Errors in diagnosis may frequently be cleared up by "X" rays,—phthisis is not infrequently diagnosed as aortic aneurism, while aortic aneurism is still more frequently mistaken for pulmonary phthisis.—B.M.J. ii./10,1575.

X-Ray diagnosis of gastric ulcer. There are two distinct methods:—

(1) *The indirect or Continental method*, in which screen examination is used to obtain information as to abnormalities of function, such as variations in tone, peristalsis, etc. An essential point of technique is rigid routine as regards the nature and quality of the meals, times of examination, etc.

(2) *The direct method*, by which the actual deformity of gastric contour produced by the ulcer is shown on serial plates. This is preferable and more reliable.

The essential points of technique are (a) the employment of a

fluid meal which will hold Barium in good suspension, and readily fill small irregularities; (b) ultimate reliance on radiograms instead of on the screen image. The diagnosis of gastric ulcer depends on the presence of a constant deformity of the gastric outline, not due to other organic lesions, which may be (i) a projection from the outline, *e g.*, a niche or an accessory pocket (ii) a defect in the outline, *e g.* a filling defect, (iii) organic hour-glass deformity (iv) pyloric stenosis. The essential quality for diagnosis of an organic lesion is the constancy of the abnormality. Spasmodic deformities present great difficulties to the radiologist, but Belladonna, *given to physiological effect*, nearly always produces relaxation of a spasm, which is not due to organic gastric lesion.—J. Magnus Redding, Proc. Roy. Soc. Med., 15, 1922 8.

Radiographing joints. Chronic arthritis in a deep-seated joint such as the hip may be demonstrated, and gouty and other chronic inflammations may be discovered.

ARTHRITIS.—"X" rays the most accurate means of diagnosis at present.—Rheumatoid arthritis and osteo-arthritis pathologically distinct.—R. Morton, B.M.J. ii./12, 481.

Gas in Tissues (formed by *B. Aerogenes Capsulatus*, etc.) can readily be located by "X" rays. It appears as black patches in skiagrams. Radiographs assist in operations for securing free drainage.—B.M.J. i./17, 8.

X-Rays in the diagnosis of gastro-intestinal disorders.—A. C. Jordan. Pr., Feb., '26, 153.

Discussion on the fallacies of X-rays in abdominal diagnosis.—B.M.A. Ann. Meeting, B.M.J. ii./28, 249.

The value of the opaque meal in diagnosis of diseases of the intestinal tract.—Sir T. Horder, B.J.R., Mar., '29, 97.

CEREBRAL TUMOURS, Localisation of, by X-rays and use of a gyrometer.—A. P. Bertwistle, B.M.J. ii./26, 631.

LUNGS AND PLEURA. Value of X-Rays in diagnosis of diseases of.—David Lawson, Pr., Feb., '26, 132.

EYE OR ORBITAL REGION. A simple apparatus and method for determining the exact location of radiopaque bodies in, by radiography.—Maj. D. B. McGrigor, B.J.R., Mar., '29, 126.

AMŒBIC INFECTION IN THE LARGE INTESTINE. Preliminary report on the value of the Röntgen ray in estimating the extent of.—J. J. Valarino, Int. Conf. Trop. Am., '24, 357.

X-Raying of Teeth.

The degree of dental infection cannot be judged simply from the radiogram. The existence of apical rarefaction is not enough to condemn a tooth, and the assumption is refuted that these rarefied areas denote a menace to health proportional to the degree of bony absorption.—L. ii./25, 942. See also *ibid*, 994, 1094.

X-Rays, Diagnostic Uses of.—W. I. Bruce and J. Magnus Redding, Dict. of Pract. Med., 1921.

X-Rays and diagnosis.—C. Thurston Holland, J.R.S., '23, 123.

METABOLIC CHANGES ASSOCIATED WITH X-RAY AND RADIUM TREATMENT.

X-Rays in massive doses produce lowering of urine excretion and definite Chloride retention, when upper abdomen is rayed. With radiation of upper abdomen, where previous Chloride excretion is low, there is a tendency to sickness (cases reported). This can be prevented by preliminary feeding with Sodium Chloride daily, so that Chloride excretion is raised to 10 or more Gm. per day before treatment is commenced and continued during administration.—A. T. Cameron and J. C. McMillan, L. ii./24, 365. Exactly similar results found in patients treated with X or gamma rays. Changes in metabolism found to vary with site radiated. Three cases of X-Raysickness examined

failed to show change in metabolism—sickness apparently psychic. Cases treated with Calcium Chloride, etc., before radiation (some with Sodium Bicarbonate) showed less reaction.—E. C. Dodds and J. H. D. Webster, *L. i.*/24,533. See also *Arch. Radiol.*, '24,29,140.

ENZYME ACTION. Radiation has practically no effect on.—P. D. Lawrence, *Arch. Radiol.*, 26, 244.

Simple and inexpensive apparatus for making serial radiographs of the pylorus and duodenum.—*Arch. Radiol.*, 26, 249.

Effects of X-Rays on different wave-lengths upon some animal tissues—proof of DIFFERENTIAL ACTION. About 6 times as much short wave-length energy as long wave-length energy must be expended in a layer of skin to produce equal reactions and this factor falls to about 2.6 in the case of a tumour—experiments on rats.—Prof. S. Russ, *J.R.S.*, Jan. '24.

X-Rays cause a gradual and regular lowering of the blood pressure in animals.—M. B. R. Swann, *Arch. Radiol.*, '24,29,195.

FIRST BILINGUAL CONGRESS OF RADIOLOGY PHYSIO-THERAPY, London. Discussions on the normal stomach 'an extremely elusive thing,' method of examination and on deep seated therapy also on use of Radium and H.F. Currents, *B.M.J.*, i./22,958.

First International Congress of Radiology. Reference to the pioneer work of the younger generation.—*B.M.J.* ii./25,72. See also *B.J.R.*, *Apl.*, '27.

Three periods of X-Ray therapy can be traced: (1) the period of inadequate and tentative dosage; (2) the period of the ushering in of the Coolidge tube and the intensive Erlangen technique, and (3) the period dating from the recognition of the failure of Erlangen methods and the use of the power of the modern tube in divided doses.—W. Sampson Handley, *L. i.*/29,2.

General Reviews of Treatment.

A summary of "X" ray therapeutics with description of technique, skin affections, enlarged lymphatic glands, exophthalmic goitre, disease of the blood, and ductless glands, diseases of the pelvic organs, malignant disease.—R. Knox, *L. ii.*/19,183.

Treatment of lupus, rodent ulcer, and other skin affections with "X" rays and the Finsen Light and the two combined, are carried out with satisfactory results. The mode of action of "X" rays is not bactericidal. They appear to act by retarding osmosis and causing a slow degeneration of the cellular structure, probably due to leucocytosis. Lupus vulgaris, especially the ulcerative form (on ulcers the drying effect is most marked), serofuloderma, tuberculous osteitis, and tuberculous glands, rodent ulcers, epithelioma, keloid, sarcoma, lupus erythematosus, acne rosacea, actinomyces, mycosis fungoides, naevi, eczema, psoriasis, acne, favus, syeosis, ringworm, and hypertrichosis have been satisfactorily treated by "X" rays. The rays cause the absorption of œdema.

Treatment with X-radiation is of value after operation to prevent recurrence in some forms of malignant disease.

The effect of large doses of X-Rays upon the general condition. In nearly every instance marked debility and malaise appeared similar to that following intoxication. This condition is quickly improved by hypertonic solutions of Sugar, Sodium Chloride or Sulphate. Investigations show that not only is Sodium Chloride largely eliminated from the blood after a strong dose of X-Rays but that the concentration of Potassium, Calcium and Cholesterol is profoundly altered, while the blood sugar reacts sharply.—*L. ii.*/23,353.

Radiology has helped in establishing the truth of FOCAL SEPSIS—in diagnosis of sinus infection, for example; it permits of seeing the morbid condition of an antrum or some other accessory nasal cavity; in mastoid infection the same experience obtains; in dental sepsis, it is our chief stand-by in assisting diagnosis. As other instances of focal sepsis established frequently by X-Rays, one may point to the chronically inflamed appendix, and the chronic inflamed gall-bladder. An important matter is, of course, the radiology of the HOLLOW VISCERA. It is scarcely an exaggeration to say that the whole of our present conception of the neuro-muscular mechanism of the alimentary canal is the result of X-Ray revelations. Need for combining radiographic and clinical investigation. The ideal radiologist should be a clinician in spirit and (it is inferred) a pathologist in spirit also. With regard to Radiotherapy, the paper is hopeful in dealing with cancer. Cancer is

controllable.—From the Mackenzie Davidson Memorial Lecture by Sir Thos. Horder, J.R.S., Oct., '24.

In X-Ray treatment of the PELVIC ORGANS, the genu-pectoral or Trendelenburg position, whereby the small bowel is removed out of the field, may be employed with advantage, since it is held that grave constitutional reactions depend upon damage to the mucosa of the small intestine. It seems probable that acute constitutional symptoms are due to flooding of the circulation with proteins liberated by the destruction of cells. When the symptoms have appeared, elimination of the toxic proteins may be assisted by diuresis, plenty of fluids being given by the mouth. Lange reports benefit from the administration of Sodium Bicarbonate before and after radiation. A red blood count below four millions and a low blood pressure are indications that X-Ray therapy should be conducted with caution.—H. Rolleston, J.R.S., '23, 5.

Electro-therapeutics—a survey.—S. Melville, L. i./25,61.

The following are arranged in an approximate alphabetical position:—

Acne successfully treated with vaccines combined with all wave-length radiations.—R. Knox, Arch. Radiol., 1921, 26, 60.

Initial effect is increase of inflammatory activity, but the subsequent benefit is pronounced.—J. H. Sequeira, B.M.J. ii./24,514.

The best local remedy for acne, eczema, seborrhœic dermatitis and lichen planus. Unsatisfactory in rosacea except for its effect on the acne-like lesions. In psoriasis should be used with caution and only in selected cases. Its action in ringworm and favus is brilliant, and results are good in sycosis and folliculitis.—Pres., Oct., '24, 342.

ACNE.—X-Rays usually successful. Radiologist must have experience in therapeutic dosage—2/3 Sabouraud Pastille free from danger and may be repeated in three weeks.—H. G. Adamson, L. i./25,401.

Adhesions and fibrous bands, resulting from bullet wounds, relieved by filtered X-Rays (through Aluminium 0.5 mm. thick). Results good.—A. Winkelried Williams, B.M.J. ii./16,754.

Angina Pectoris.

A spark-gap equivalent of 25 cm., a 6 mm. Aluminium filter, an intensity of 2.5 m.a., and a skin anti-cathode distance of 30 cm. Two fields are irradiated, a precordial one of 20 cm. diameter over the internal part of the third left intercostal space, and a dorsal one of the same diameter over the third dorsal vertebræ. The thyroid is protected by an opaque covering. Three treatments are given weekly—the first week 5 minutes and a dose of 100 R. units over each field, and in each three succeeding weeks the duration is increased by 5 minutes and the dosage by 100 R. units at each treatment—a total of 2,000 R. units in the 4 weeks. Great, and usually lasting, benefit obtained. Contraindicated in debility, marked cardiac insufficiency, and in people over 70.—G. Lian and M. Marchal, Paris Med., Dec. 1/28, per B.M.J.E. i./29,9.

Blood Affections:—

LEUKÆMIA.—In some forms, advantageous (myeloid, chronic lymphatic). Diminished size of swollen organs, increase in weight and delay in recurrence. Complete cure never effected.—L. i./09,507; B.M.J. i./09,1299. Rays of fairly high penetration should be given. Screen 0.5 to 0.8 mm. thick. Dose 6H to 8H once every two or three weeks, or a smaller one more often.—B.M.J. i./11,985. The treatment may do so much damage to the liver as to cause cirrhosis. Cure of the leukæmia, but death after a year from cirrhosis and ascites.—B.M.J. i./09,1236.

Enlarged lymphatic glands amenable to treatment.—B.M.J. i./09,1299.

Likely to be useful in diseases with hyperplasia, rather than hypoplasia, of the blood elements; in the leukæmias, rather than the anæmias.—G. Lovell Gulland, B.M.J. ii./21,71. See also J. Metcalfe, B.M.J. ii./21,273.

In general, results of treating morbid conditions of the blood disappointing.—R. Knox, Arch. Radiol., 1921, 26, 60.

Some effects of X-radiation on blood.—W. V. Mayneford, B.J.R., Aug., '28, 257.

ERYTHAEMIA (splenomegalic polycythæmia) well treated by X-Rays, Blood data markedly improved.—E. J. Stolkind, L. i./23,1312.

POLYCYTHAEMIA RUBRA.—A case successfully treated by X-Rays. Suggested that the method may also be useful in some cases of high blood pressure.—S. W. Patterson, L. ii./25,1112,1131.

Bronchial Asthma. Some cases cured by irradiation of the lungs with X-rays and later by exposure of the spleen to X-rays.—Arch. Radiol., '24, 29, 307.

In really bad cases the results of X-irradiation are often spectacular. Possible metabolic influence on the ductless glands. There is remarkable increase in body weight and general feeling of well-being. The field includes the whole trunk, the abdomen being the important area. The tubes are centred over the epigastrium and a corresponding point posteriorly. Voltage not above 170,000, with a filter of 3 mm. Aluminium. Treatment given twice weekly in bad cases and once weekly in average cases, 4 to 6 being the course. No blood changes and only slight nausea in a few cases. Might prove of value in whooping cough.—S. G. Scott, Congress of Radiol., Stockholm, July, '28, L. ii./28,352.

Two Coolidge tubes, one focussed on the back and the other on the front, arranged for the rays to cover the whole trunk, are energised by two separate installations, both tubes running at the same time. The anterior tube, 12 inches from the skin, is centred over the epigastrium and arranged to cover an area from the chin to the symphysis pubis, and the posterior tube a corresponding area. Voltage should never exceed 150,000 volts. 3 to 4 mm. Aluminium filters are used—2 mm. with a corresponding small dose for children—the average dose for an adult being 15X per 3 mm. Aluminium, back and front. Using a 25 cm. spark-gap (points) and 8 mm. through the tube, this takes 5 minutes. The dose is given twice a week for 4 weeks, then 2 weeks' rest, then two laterally once weekly. Measure the dosage by a Sabouraud pastille placed on the skin, the tint being read by means of a tintometer—a quarter Sabouraud B tint, measured on the skin without a filter, equals a full erythema dose.—Good results in 89 out of 121 cases.—S. G. Scott, B.M.J. i./29,10. See also B.M.J. i./26,939.

Bronchial asthma and chronic bronchitis without asthmatic attacks markedly benefited by Röntgen-Ray treatment.—I. Gerber, JI.A.M.A. ii./25,1029.

Forty-six per cent. of 26 asthmatic patients completely cured, and 38% much improved, by radiotherapy, the spleen being irradiated with half the skin dose of penetrating Röntgen Rays.—Per JI.A.M.A. ii./25,1098.

Carbuncles respond quickly to X-Ray therapy.—P. Cave, B.M.J. i./29,664

Specific in the majority of carbuncles, when inflammation is limited to the skin and subcutaneous tissues.—F. M. Hodges, JI. A.M.A. ii./25,1293.

Cheilitis exfoliativa. Several striking successes from X-Ray therapy—J. H. Sequeira, B.M.J. ii./24,513.

Chronic Cough of Children.—Indications for use of Röntgenotherapy in.—Per JI. A.M.A. ii./25,1331.

Diabetes. Two cases recorded in which the internal secretion of the pancreas was stimulated by X-Rays sufficiently to reduce the glycosuria and raise the carbohydrate tolerance.—per Pres., Oct. '23, 233.

Eczema. Can cure. Give small dose each time—less than enough to turn the Sabouraud Pastille—about 7 to 10 minutes according to the tube. Anode 6 inches from the skin (protected by four layers of blanket) $\frac{1}{2}$ to 1 m.a. is run through the secondary. 48 cases—14 cured, 22 much improved. Suitable for early cases and acute ones in which operation is feared. Take care to prevent dermatitis.—F. A. Stoney, B.M.J. ii./12,476; L. i./13,590.

In the knowledge of the writers, a young woman was completely cured of eczema by 2 months' treatment with X-rays, after her case had been practically despaired of. She herself had got to the stage when she did not mind whether anything did her any good or not, and her own friends prayed that she might die. Drugs, in the way of local applications, had been tried over a number of years, but the effect was merely temporary and transient. (See also *Skin*).

Erysipelas.—Probably of definite value in early stages.—F. M. Hodges, JI. A.M.A. ii./25,1293. Average time for clinical cure three days, as compared with an average of more than 9 days in those treated by routine procedure.—B.M.J. E. i./27,64.

Exophthalmic Goitre. Some cases greatly benefited.

Probably large doses essential to cause partial atrophy. Medium rays should be used, 0.3 mm. Aluminium screens and a dose of 6H to 8H once in two or four weeks.—B.M.J. i./11,985.

Excellent results with radiation treatment, which should extend over long periods.—R. Knox, Arch. Radiol., 1921, 26, 60.

A prolonged course of treatment by X-rays or Radium found one of the most reliable means of treatment of exophthalmic goitre.—G. R. Murray, B.M.J. i./22,906; L. ii./23,294. A. J. Walton considers X-ray treatment very unsatisfactory.—L. i./23,271.

A method of attempting to half 'saturate' the thyroid with cumulative doses.—J. H. Douglas Webster, B.M.J. i./26,985.

62 cases out of 100 cured and able to follow usual occupations.—Maurice Hayes, L. i./26,812.

Of 57 cases treated, 30 are now quite well, 13 are much improved, 5 cases improved, 5 unimproved or worse and 3 had recurrences; there was one death. Risk in expert hands slight, but possibility of hypothyroidism.—G. Forssell and O. Sandström, Congress of Radiol., Stockholm, July, '28, L. ii./28,352. A questionnaire showed that of 5,400 cases so treated 73% were cured, 16% improved, and 11% unimproved. Figures comparable with those obtained in surgery, with the added advantage of no mortality due to the treatment.—A. Soiland and others (Los Angeles), *ibid.*

Furunculosis in infants. Results favourable; best to use soft ray and no filter.—G. G. Grules and C. B. Rose, per J1. Trop. Med., Mar. 1, 23,82.

Gynæcology.—"X" ray treatment may be offered to a patient with contracted pelvis as a substitute for oophorectomy, *i.e.*, to produce atrophy of the ovaries. Many tumours of the ovaries, *e.g.*, early stages of proliferating cystoma might be beneficially treated by "X" rays.—B.M.J. ii./09,461.

Venereal sores treated. Results valuable.—B.M.J. i./09,464.

Uterine fibroids treated by X rays.—J. D. Harris, B.M.J. ii./19,376.

Treatment of the Pituitary and Thyroid glands by the application of a sedative or regulating dose of X-Rays exerts a restraining action on the endocrine glands, bringing about, indirectly by way of the nervous system, a disappearance of climatic symptoms.—G. Holzknecht, Arch. Radiol., '24, 29, 293.

Hair—Alopecia Areata.—Small doses, *e.g.*, 1H or 2H, once in two or three weeks.—B.M.J. i./11,985.

Hyperidrosis.—Face, hands, armpits, feet, etc., 20 cases (9 being medical men) cured by "X" rays. Six sittings, one pastelle dose each, at intervals of one month is the best treatment. In two cases a cure was obtained by two sittings. The rays produce an effect on the sweat glands, and either stop their action entirely or reduce it to less than normal.—B.M.J. ii./10,522; L. ii./11,433.

Use Medium Rays without Screen, 5 H. Once in 4 or 5 weeks for several days suffices.—B.M.J. i./11,985.

The rays have a distinct influence on the sweat glands, without the production of a reaction sufficient to cause atrophy.—J. H. Sequeira, B.M.J. ii./24,514.

Hyperidrosis readily controlled.—R. Knox, Arch. Radiol., 1921, 26, 60.

Intestinal Stasis, Chronic—Radiology in.—A. C. Jordan, L. i./20,756.

Keratitis (interstitial) syphilitic. Weak doses shorten early stages of infiltration. The younger the patient the better. Striking results as to pain, photophobia and lachrymation; opacities in young subjects benefited. No damage to eye or surrounding tissues; use as an adjunct to anti-syphilitic and general treatment. Trial justified in certain chronic eye diseases, *e.g.*, painful blind glaucomatous eye and scleritis of the aged.—T. L. De Courcy and J. H. Mather, B.M.J. i./24,12. See also Arch. Radiol., '24, 29, 105.

Leprosy.—Nodules removed by repeated exposures.—J. H. Sequeira, B.M.J. ii./24,513.

Lupus vulgaris treated with fair success with Ultra-violet radiation, combined with X-Rays only occasionally in well-measured doses, care being taken not to over-stimulate the tissues.—R. Knox, Arch. Radiol., 1921, 26, 60.

In the **ulcerative** form of lupus and in scrofuloderma, X-Rays of great service. Danger of lupus carcinoma due to prolonged X-Ray treatment of dry lupus. (This point was stressed by all the speakers in the discussion, and a resolution was unanimously passed to be forwarded to the Ministry of Health, advising that a warning as to this danger should be issued to all tuberculosis officers.)—J. H. Sequeira, B.M.J. ii./24,513.

Malaria.—Better results than Quinine. The idea is that malaria is fought by leucocytolysis rather than by phagocytosis, and that this is largely carried out by the action of the spleen, which is stimulated by X-Rays. 61 cases treated.—all definitely cured.—J. J. Manoukhine, La Vic Médicale, per B.M.J. E. i./24,83. See also J1. Rontg. Soc., Jan., 1920, p. 3.

Malignant Disease :—

*Treatment has made great strides in the past few years owing to adoption of intensive methods with rays of great penetration. The original **Erlangen technique** has been modified, but the principle of a "lethal dose" (see below) to all tumour cells is maintained. By means of the very penetrating radiation, suitably filtered, tumours situated at any depth can be attacked. Of great value in inoperable cases, and offers increased prospects of immunity from recurrence if used prophylactically after removal of operable tumours. See also C. Saberton, B.M.J. ii./18,357.*

IMMUNITY TO TUMOUR GROWTH.—Animal experiments showed that some degree of immunity may result from irradiation of a tumour, but to ensure this is of great difficulty. Further, the treatment of a patient with irradiated tumour cells, after surgical removal of growth, may help to set up a state of resistance. This latter had been carried into effect in 30 cases.—H. Chambers, T. H. Kellock and Co-workers, L. i./22,212 to 219.

BREAST CANCER.—By an adequate dose of radiation, a mass of cancer cells can be killed. Russ's experiments with irradiated tumour substance. Numerous cases treated with buried Radium.—W. S. Handley, B.M.J. i./21,37.

Useful as an adjunct in cancer of the uterus, but it cannot replace operation, —B.M.J. E. i./24,27. In cases suitable for operation, hysterectomy performed. after apparently successful Radium treatment, offers patient, almost without danger, a double prospect of cure.—*ibid.*

If animal tumour cells are irradiated with almost a **lethal dose** their descendants will not be so sensitive to the same dose, if it is repeated some time afterwards, and eventually the tumour cells may become extraordinarily resistant to the rays. **Lethal dose for tumours** defined as that dose which it is necessary to give the tumour outside the body so that when it is inoculated into susceptible animals it fails to grow. If a certain time of exposure to X-Rays produced 50% reduction in tumour growth, this time had to be increased about 33% in order to be lethal. Tumours irradiated to a less extent than was necessary for lethal action acquired a resistance, one strain of tumours having required 2.5 times the ordinary exposure to X-Rays before a lethal action was obtained. As a result of an immunity operation, consisting in irradiation of a tumour removed, and then re-introduced into the body of the patient, it was found that wherever these tumours had been given twice the lethal dose effective for animal tumours they failed to grow. The factor of two has been decided on as a measure of safety.—Prof. Russ, L. i./24,592; B.M.J. ii./24,105.

General survey of radiography in malignant disease.—S. Gilbert Scott, B.M.J. i./25,596,601.

CARCINOMA OF THE BREAST.—Low-voltage prophylactic treatment, embracing practically the whole trunk, seemed to extend the range of control of the disease.—G. Scott, L. i./25,661.

Prophylactic post-operative treatment should extend over months. High voltage technique to be substituted for low voltage when a small recurrence detected.—J. H. D. Webster, L. i./25,661

Radiological treatment in Stockholm of cancer of the female pelvic organs. Cancer of cervix shows improvement of symptoms; also details of the treatment of cancer of the corpus uteri, ovaries, vagina, urethra, and vulva by filtered (3 to 4 mm. Lead) Radium radiation.—J. Heyman, B.M.J., ii./25,827.

Morphine is not an ideal analgesic in malignant disease. Judicious X-ray treatment will keep the majority of cancer patients free from pain until at most a few weeks from the end, while often mitigating other symptoms such as hæmorrhage and discharge.—F. Hernaman-Johnson, Pr., Apl., '26,315.

As regards cancer of the breast, recent papers at German X-Ray Congress indicated that intensive penetrating rays are positively harmful. Rays of moderate penetration satisfactory.—L. i./26,1153.

The effect of irradiation of non-malignant and malignant tumours is much increased if preceded and followed by **intravenous injections of Glucose 30% Solution**, 10 Cc. doses being made shortly before each irradiation.—G. Holzknecht, B.M.J. i./26,534.

The action of radiation on the blood-supply of tumours.—J. C. Mottram, L. ii./28,966.

Granulomata—Striking results.—J. H. Sequeira, B.M.J. ii./24,513.

Value of X-Rays in various forms of malignant disease.—F. H. Johnson Pr., Nov., '24,342.

Mastitis, Chronic.—X-rays the most effective agent, but are ineffective in the cystic form, may aggravate the subacute form and are contra-indicated in acute mastitis.—W. Sampson Handley, L. i./29,1.

Menorrhagia treated by intensive X-Ray therapy.—Louisa Martindale, B.M.J. ii./23,411. See also *Gynaecology, antea*.

Moles (Naevi).—Medium Rays, without screen (or only 0.1 mm. of Aluminium). Give 3H or 4H once a fortnight. A number of sittings required. Radium gives more excellent results and is easier to apply.—B.M.J. i./11,985.

HAIRY AND PIGMENTED MOLES, e.g., on face, usually improve—hair can be removed and pigmentation lessens. Use fairly large doses. Medium penetration. No screen—5H or 6H once in 3 to 5 weeks. Many doses may be required—must not produce a violent reaction.—B.M.J. i./11,985.

Parotid Gland Infections, Chronic, respond well.—F. M. Hodges, JI. A.M.A. ii./25,1293.

Poliomyelitis well treated—JI. A.M.A., June 7/24,1847, Pr., Aug., '24,134.

Prostatic Hypertrophy.—Good results obtained.—B.M.J. E. i./25,80.

Pruritus ani and pruritus vulvæ relieved by a few exposures. Benefit usually after first; unwise to persist if no speedy relief.—B.M.J. ii./24,513. See also L. ii./11,510; B.M.J. ii./11,826.

Psoriasis.—Psoriasis and other skin affections, action of "X" rays in.—A thorough consideration of suitable dosages.—S. Ernest Dore, B.M.J. ii./13,1016. See also B.M.J. i./11,985, and C. E. De Silva, B.M.J. i./18,9.

Where eruption is limited, occasional treatment of value. In some cases of seborrhoeic dermatitis, X-rays have a rapid beneficial effect; moist lesions dry up; scaly lesions disappear.—J. H. Sequeira, B.M.J. ii./24,513.

Complete cure in 85% of cases can be had by employment of Roentgen Rays alone.—JI. Radiology (Am.), Oct. '25, per JI.A.M.A. ii./25,1670.

Ringworm.—If extensive, "X" rays best treatment, afterwards "finishing off" with Croton Oil.

Single dosage method harmless. Severe dermatitis followed by permanent baldness is the result of over exposure.—MacLeod, L. i./09,1373. The hair is several months in growing. In a large majority of cases it is necessary to irradiate the whole scalp. This by 10 or 12 exposures necessitates upwards of four hours. By dividing the scalp into rectangular areas, and irradiating each (surrounded by a lead foil sheet) in succession, the time is reduced to 2½ to 3 hours.—L. i./09,1378.

It is usual now to use the FIVE AREA METHOD without shielding with lead foil. The oblique incidence of the rays on those parts where the areas overlap results in an epilation dose only being given to the entire scalp.

Great care should be taken not to exceed dose required to produce **temporary epilation**. Dose of 5H with rays of medium penetration (4 to 5 in. equivalent spark gap). No screen and one dose only. Danger of producing permanent partial baldness.—B.M.J. i./11,985.

Further Refs. in 18th Edn., Vol. II., p. 301.

Unfiltered X-Rays from a hard tube good in ringworm. Filtration through Aluminium not advantageous.—C. J. McSweeney, B.M.J. ii./26,670.

Rodent Ulcer.—Continue treatment till all raised edges, however small, disappear. 6H should be given once in three or four weeks, or 2H once weekly. Medium rays and no screen.—B.M.J. i./10,423; i./11,985.

An ulcer of 25 years' duration healed by treatment three times a week (10 minutes' treatment every second day). Small ulcers not involving bone or cartilage cured by three exposures of a two-hours' duration to a half-strength Radium plate. 1,262 cases treated.—J. H. Sequeira, B.M.J. ii./24, 513.

Rodent ulcer treated by X-radiation.—F. Hernaman-Johnson, L. i./26,389.

Sclerosis, Multiple.—Of 28 cases, 22 showed more or less definite improvement up to clinical cure. Treatment given in 7 sittings: at intervals of 1 to 2 days the skull is irradiated 3 times, the neck once, the chest twice, and the sacrum once, and this series is given 10 times a year, the whole course being repeated after an interval of 6 to 12 months. Hard rays employed, filtered through 4 mm. Aluminium, and dose not exceeding 25% HED measured on the skin.—K. W. Ipatow and A. Romanowa-Leskowa, Congress of Radiol., Stockholm, July, '28, L. ii./28,352.

Skin Affections treated by X-Rays more safely than by Radium in the matter of overdose. The further progress of an incurable rodent ulcer can be

delayed for years by X-Rays, but not by Radium. Indurations, itching, chronic infiltrations, lichenification, conditions requiring depilation, and new growths treated.—E. W. Reed, B.M.J. ii./22,559.

ORIENTAL SORE treated with X-Ray applications and Potassium Permanganate—the latter packed round the sore, after removing scab and cleansing base of the ulcer. Antim. Tart. injections.—M. L. Treston, L. ii./21,270.

Of 30 patients only 1 did not heal within 30 to 120 days, but scar more conspicuous than with Salvarsan or Antimony.—B.M.J.E., '29,48.

Suppuration, persistent—Influence of X-Rays on.—E. P. Cumberbatch, L. i./14,1392.

Tuberculosis, Pulmonary.—A plea for X-Rays in diagnosis and prognosis.—Pres., Aug., '23,288.

Whooping Cough.—Striking effects. A fairly large dose, preferably a single exposure over the chest.—B.M.J.E.i./24,61. B.M.J.E. ii./24,78.

Reduced bronchial glands.—B.M.J.E. ii./24,90. No true benefit: temporary results.—H. K. Faber and H. P. Struble, Jl. A.M.A. ii./25,818.

Erlangen Technique.

Malignant Disease.—An intensive form of X-Ray treatment, with which is combined, in a number of cases, a prolonged exposure to ionisation, a copper solution being used. Exposures last from 6 to 8 hours. On the day following ionisation, there is 5 to 9 hours' X-radiation—with opiate.—R. Knox, L. i./22,1131, see also *ibid.* 551.

CANCER (especially of UTERUS).—A large single dose directed towards the primary lesion. The instrument consists of a twin-coil installation capable of giving high voltage in the secondary. (Estimated at 180,000 to 200,000 volts. An X-Ray tube capable of continuously passing a current of 2.2 m.a. at that voltage).—R. Knox, B.M.J. ii./21,267; ii./22,678.

UTERINE AND MAMMARY CANCER.—Good results.—R. Morton, B.M.J. i./21,173.

See also J. Curtis Webb, B.M.J.i./22,92. H. Kingsley Ward, L. i./22,366; W. Pilger, L. i./23,115; R. Morton and H. B. Lee, *ibid.* 117.

By the projection of several narrow pencils of rays as above and the FRANKFURT method (broader pencils of rays) great strides have been made. Treatment of uterine hæmorrhage reduced from 3 to 6 months to two applications on two consecutive days, due to the fact that a harder, *i.e.*, a shorter wave, is applied.—C.D., Dec., 6/24,826.

Developments in deep Radiotherapy.—N. S. Finzi, B.J.R., Apl., '25,67.

Results favourable in selected cases.—L. Cassidy, B.M.J. i./25,458.

LEUKÆMIA.—Effect of deep therapy on the blood.—W. L. Watt and J. C. Braine, L. i./25,6.

The treatment of splenomedullary leukæmia. John Gracie, Pr., l., 'Ap26,320.

Myeloid leukæmia well treated.—per Pr., Apl., '26,331.

The Erlangen results were not reproduced by others, many patients suffered from the destruction of red cells and in some cases death followed. The original Erlangen treatment proved unsuited to the majority of cases in this country and most workers divide up the large doses over several days.—L. i./26, 1153.

'Massive' and 'Hypermassive' radiation in skin cancers.—W. A. Evans, B.J.R., Nov., '28,396.

Dosage.

The X-Ray Unit Committee, meeting during the **Second Internal Congress of Radiology**, held at **Stockholm in August 1928**, made the following recommendations which were unanimously adopted by the Congress.

That an international unit of X radiation be adopted, this unit to be the quantity of X radiation which, when the secondary electrons are fully utilised and the wall effect of the chamber is avoided, produces in 1 Cc. of atmospheric air at 0° C. and 76 cm. Hg. pressure, such a degree of conductivity that one electrostatic unit of charge is measured at saturation current: that this **international unit** be called the "**Rontgen**" and be designated by the **letter R**; that various standard methods be employed to establish the unit: that for all comparative purposes, it is advisable to employ ionisation chambers which have been calibrated in terms of a standard chamber for X radiation of the various qualities employed: also advisable

to make the wall effect of these chambers as small as possible: that the instrument used to measure X-Ray output be called a dosage meter: that the constancy of the indications of the dosage meter be tested by means of gamma radiation emitted from a definite quantity of Radium element, the measurement being carried out always under the same conditions. That any specification of dosage is incomplete without specifying the quality as well as the quantity of the radiation: for practical purposes the quality may be expressed by stating the half-value layer in a suitable material, or by stating the effective wave-length, as determined on the percentage amount of radiation transmitted through a given thickness of a suitable material (Copper or Aluminium).

These recommendations were regarded as provisional, subject to modification later in the light of further information.

It will now be possible for a **radiologist in one country** to **reproduce accurately an X-Ray dose** and thus be enabled to compare his results with those of other radiologists in other countries.

The International X-Ray Unit Committee has been authorised to continue its deliberations and submit a further report for consideration at the next Congress in 1931.—L. ii./28,285.

Sabouraud's Pastelles consist of Bristol paper coated with an emulsion of barium platinocyanide in amyl acetate collodion. The alteration in colour caused in these pastelles at half distance, *i.e.*, $7\frac{1}{2}$ Cm., is observed and forms the basis of the dosage.

In this apparatus a pastelle of 1 colour only is used (*cf.* Holzknicht's *infra*). This represents the same dose as 5 on the Holzknicht scale. The machine is cheap, but indicates one dose only—*viz.*, 5H.—B.M.J. i./11,986.

The Pastelle is suitable for measurements if it is recognised that the dose registered as one Sabouraud dose is not the full biological dose when one comes to the shorter wave-length. In Germany an instrument employed in which the current through a small ionization chamber is amplified by an electronic valve, and measured by a galvanometer.—N. S. Finzi, J.R.S., Oct., '23, 171.

Holzknicht's Chromo-Radiometer. In this a 'pastelle' changes color under the influence of the rays from a canary yellow to brown. The graduated scale shows various tints numbered from 3 to 24. The unit 'H' is that amount of raying needed to change the color of the pastelle from one tint to the next,—this indicates '1H.'—B.M.J. i./11,986.

There are further the radio chronometer of Benoist, the quantimeter (*vide* below) of Kienbock and the method of Milton Franklin by measuring the ionisation of the air produced by the radiation from the "X" rays.

The "**Wehnelt Radiometer**" consists of a silver strip, the same thickness throughout, and an aluminium strip, tapering in thickness, mounted side by side. These are moved across the slide in front of a fluorescent screen so that the lower half shows the shadow due to the Silver, and the upper half to the Aluminium. When the appearance of both halves are alike, the position is read off on a scale, and this is accurately proportional to the penetration of the tube.

The **Kienbock Quantimeter** consists of strips of Silver Bromide paper and is exposed, developed, and then compared with standard scale. The spot where the tint agrees gives the value of the tube.

"X" Units given by this apparatus are $=\frac{1}{2}$ H, *i.e.*, $10X=5$ Holzknicht Units or the Sabouraud Tint "B."—B.M.J. ii./12,474.

Measurement of Current through "X" ray tube—A milli-ampere-meter can be used to measure the current passing through the "X" ray tube, the production of rays bearing a close relationship to the current so measured. Photographs taken with different currents through "X" ray tubes are identical when the times of exposure are so adjusted that the figures obtained by multiplying currents by time are equal—*milliampere seconds*.

To measure the effective current through a tube the currents in the wrong direction are to be eliminated, *e.g.*, by aid of the **Villard Valve Tube**. This is arranged in series with the "X" ray tube. Several valve tubes in series are generally necessary to rectify the heavy currents used in modern radiography and radiotherapy.

A Mechanical Rectifier may be used instead of valve tubes.

Dose.—The means of controlling the penetration are in the main the regulation of the vacuum for 'hard,' 'medium,' or 'soft' rays. For regulating

the vacuum self-regulating tubes are used. *Screens* are used to absorb the softer rays—that is, those whose chief effects are on the skin, when the object is to affect deep structures. They may be made of wash-leather and gelatin; *Sheets of Aluminium* 1 mm. in thickness superimposed on one another, the number used depending on the effect desired, are also employed. **Copper and Zinc Filters** are used in deep therapy.

A *small dose* temporarily stimulates epithelial structures, increases secretion from the sweat and sebaceous glands and increases vigor of hair growth. A *full dose* may be followed by a slight erythema after a latent period of some ten days. Hair becomes pale and drops out,—but growth starts again some 6 to 12 weeks afterwards. A *large dose* is followed in about a week by erythema, increasing in severity. Marked inflammatory reaction sets in, and vesication takes place, necrosis follows, deep or superficial according to quality of rays absorbed. The ulceration may last for years. It may ultimately become epitheliomatous. *Repeated doses* produce results according to whether the further dose is or is not administered before the effects of the previous one have passed off.

Further Refs. and Abstracts in 18th Edn., Vol. II., p. 304.

“X” Ray Installation and work for Pharmacists.—Description of apparatus etc.—P.J. i./13,4,166.

Lectures by R. S. Wright dealing with the apparatus used in the medical applications of electricity. 1st, Medical application of low-tension currents for galvanic currents, faradisation, cautery, radiant heat, vibro-massage and ultraviolet radiation.—P.J. i./14,132. 2nd and 3rd, High tension currents in “X” ray work.—*Ibid.*, p. 212,291. 4th, Direct application of high-tension currents.—*Ibid.*, p. 402.

Harlow and Evans employ an ‘end radiation,’ as result of the radiation passing through 1cm. of Aluminium. The method crystallises itself into measuring the **percentage reduction** of intensity by this thickness of Aluminium. This reduction is unique for a definite intensity distribution and corresponds to a definite quality of end radiation.—Physical Soc. and Rontg. Soc., Feb., 23, 1923.

Martin Berry, in a paper ‘PRACTICAL MEASUREMENTS FOR MEDICAL PURPOSES,’ dwelt on adjustments of the speed of revolution of the interrupter, duration of contacts, adjustment of the self-induction, and one should be able to adjust the condenser capacity. With the apparatus at best pitch, it is still possible to increase the depth dose, *e.g.*, with absorbent matter possessing as nearly as possible the scattering and absorbing power of the human body—and capable of being moulded to the body. *Paraffin Wax* commonly used and assumed to be equivalent to the human body, but he had found that while the percentage transmitted was 34.1 with water, it was 46.6 with Paraffin.—J.R.S., Oct., '23,169.

Electric Currents, measurement of through tissues by use of the wireless thermionic valve.—G. B. Batten, J.R.S., Oct., '23,170.

Measurement of the intensity of X-Rays by the **ionisation method** and by change in tint of a **Barium Platinocyanide** pastelle.—E. A. Owen and P. K. Bowes, J.R.S., '21,107.

Measurement by a **BALANCE METHOD**.—S. Russ and L. Clark, J.R.S., '22,154.

A discussion on International Units and Standards.—L. ii./25,94.

A **Spectroscopic Unit** for dosage.—A. Dauvillier, B.M.J. i./26,911.

Dangerous and Untoward Effects to Operators and Patients.

Testicles of rats exposed to ‘X’ rays soon contained no spermatozoa—the soft rays are the most easily absorbed by tissue—they have to be filtered out when it is required to reach deep tissues with the hard rays.—Clunet B.M.J. i./14,107.

“X” ray **Dermatitis**.—May result to hands after long exposure, relieved by application of Salicylic Acid, Menthol, Cocaine and Lanolin, Iodol.

“X” ray **Burns, Treatment of**. An operation introduced for the relief of bad cases in which painful ulceration has occurred and proved rebellious. Slight cases can be managed with fomentations, lotions, pastes and Unna's Zinc Gelatin.—A. Eddowes, B.M.J. ii./10,862

Superficial "X" ray dermatitis can be cured by Radium. Sir James Mackenzie Davidson said that in most cases of "X" ray burns of the hands the burns ended sharply at a line corresponding to the coat cuff. The cloth of the sleeve is quite transparent to "X" rays. This therefore would point to the "X" ray burns being due to a **Secondary Radiation**.

Treatment in Graves' disease showed that if pressed too fast dermatitis may be produced. A filter of 4 to 6 layers of note paper used with success. Morton employed pads of lint soaked in **Sodium Tungstate Solution** and dried.

Influence of "X" Rays on the thymus gland. Experiments on rabbits showed degeneration of lymphocytes within three hours of exposure, and within 12 to 48 hours disappearance from the gland.—B.M.J. i./11,1318

Effects of "X" rays on thyroids in rabbits.—B.M.J. i./12,28.

See also *Secondary Radiation*, p. 295.

Acute constitutional symptoms caused by "X" Rays and Radium Irradiation.—These are due to flooding of the circulation with proteins liberated by cell destruction. This can be due to damage of the mucous membrane of the small intestine. Cell destruction in other parts, *e.g.*, growths in the neck and mammary region may be followed by acute constitutional symptoms. Elimination of toxic proteins may be assisted by diuresis; give plenty of fluids *per os*.—Sir Humphry Rolleston, B.M.J. i./23,1.

Radiation Sickness.

The bugbear of the Radiologist, which may be sufficient to turn the scale against the patient. With low voltage, only treatment over considerable area seems to cause sickness, but with high voltage the sequel may follow treatment of only a small area, and the vomiting might become uncontrollable.—G. Scott, L. i./25,661.

Aplastic anaemia following X-Ray treatment.—J. M. Ross, L. i./25,867.

Cancer of the Uterus.

A warning regarding the stimulant effect of inadequate radiation.—L. ii./25, 139.

Acute X-Ray burns.—Burns are caused either through ignorance, careless technique or insufficient protection. Every doctor using X-Rays should have a diploma for such and every operator should have passed an adequate examination. *The use* of such a powerful and dangerous force *should be licensed*.—G. T. Loughborough, B.J.R., July, '25,136. A case of severe inflammation of the scalp following X-Ray treatment for ringworm—thought to be due to secondary irradiation from Picric Acid previously used for treatment.—G. B. Batten, *ibid.* 138. A 3 to 5% Cycloform ointment most efficient for relieving the pain of burns. After the acute stage treat the indolent ulcer with 3 to 4% Scarlet Red Ointment. Screening with a transformer more dangerous than with a coil. Important to have the distance of the patient from the source of illumination a *minimum of 14 ins.*—*more in abdominal cases.* Cases should *not be touched with iodine* which gives definite secondary radiation. Dr. Batten's case more likely to be due to previous treatment with Mercury Ointment than with Picric Acid.—N. S. Finzi, *ibid.* 139.

Prevention and treatment of untoward reactions following deep Rontgen ray Therapy.—H. P. Doub and Co-workers, J.L.A.M.A., ii./25,1299.

Perforation of gastric ulcer during X-Ray examination. Recovery after operation.—F. W. Lang, L. ii./26,1061.

Protection Committee, Revised Report (Dec. '23).

(Address c/o Royal Society of Medicine, Wimpole Street, London, W. 1.)

Amongst other measures, the following are insisted on:—

The bulb to be as completely as possible *surrounded with protective*. For diagnostic purposes, broadly speaking, the bulb should be enclosed as completely as possible with a material equivalent to not less than 2 mm. of lead. The material of the diaphragm should be equivalent to not less than 3 mm. of lead. The screen should be fitted with lead-glass equivalent to not less than 2 mm. of lead. A protective screen equivalent to not less than 2 mm. of lead should afford protection from scattered radiation in the case of a couch. Lead rubber gloves equivalent to not less than 2 mm. of lead to afford protection for both back and front of hand. Goggles and aprons may be advantageously worn. In "overhead" equipment, operator

should stand behind a protective screen equivalent to not less than 2 mm. of lead. Screen should be not less than 3 ft. 6 in. wide and 7 ft. high, and should extend to within one inch of the ground. Window, if provided, need rarely exceed 9×6 in., and its lead equivalent should be not less than 2 mm. For **Superficial (low voltage) therapy**. Small cubicles not advised for installing new X-ray departments. Walls, where cubicles exist, should extend from floor to ceiling. For **High Voltage therapy**. Small cubicles not recommended. Regulations as to walls and protective from bulb, as before. Great stress is laid on ventilation.—J.R.S., Jan. 24, 27 *et seq.*

Handling of Radium Emanation Tubes (Protection Committee Report, Dec. '23.) Use forceps, preferably wooden, and carry from place to place in long-handled boxes, lined on all sides with 1 cm. of lead (and in storage, 8 cm. or equivalent). Handling of *Emanation* should be carried out during its relatively inactive state.

The NATIONAL PHYS. LABORATORY (Teddington) is prepared to inspect and report on installations. The various instruments dealing with measurement of current (ammeters and milliammeters) and voltage should be standardised by the N.P.L. The Committee recommend that the plant should be provided with means for measuring secondary voltage easily, *e.g.*, by kilovoltmeter, sphere-gap voltmeter, or the like.—J.R.S., Jan., '24, 27, *et seq.*

Protective materials.—About 20 mm. ($\frac{3}{4}$ inch) of steel plate found to give protection equal to 3 mm. of lead. A Barium Sulphate mixture required 60 mm. to equal 3 mm. of lead. P. J. NEATE'S formula, one-third coarse Barium Sulphate, one-third fine, one-third cement, gave somewhat better results. The open lead-glass bowl affords no protection in many directions. Sheet-glass of lead value, 0.12 per mm. well spoken of—obtainable as thick as 18 mm.—G. W. C. Kaye and E. A. Owen, J.R.S., Oct., '23, 169.

An exhaustive study of Protective Materials at the Nat. Phys. Lab. for the Protection Committee. Numerically, 1 mm. of the following is equivalent to the stated thickness of sheet-lead in mm.

Lead Glass	..	0.12 to 0.2	Woods	0.001 or less
„ Rubber	..	0.25 to 0.45	Baryta Plaster	0.05 to 0.13
Bricks and Concrete	..	about 0.01	Steel	0.15

These are relative to Tungsten X-rays generated by 100,000 volts.—G. W. C. Kaye, Phys. Soc. and Rontg. Soc. Joint Publicn., Feb. 23, 1923.

Nitrous Acid is certainly not present in the air of the X-ray room in sufficient amount to produce ill effect upon the patient or operator. However, in unfavourable conditions Ozone may be produced in amounts as much as seven times as large as Konrich's figure for the minimum quantity (0.5 mgm. per Cc. of air), which produces exhaustion, blood changes, etc.

Rontgen gas " poisoning resembles Ozone poisoning.—J.R.S., '21, 155.

Industrial uses of X-Rays.

"X" rays were used for revealing defects in aeroplane timber—wood is very transparent to the rays.—G. W. C. Kaye & R. Knox, C.D. '19, 537. See also B.J.R., Apl., '26, 67.

Examination of materials (steels, ferrous alloys, aircraft tubes)—a general discussion held by the Faraday Society and the Rontgen Society, April, 1919. The publication contains in addition good papers on modern views as to "What are X-Rays? How formed and how produced?", "Effects," and a table showing the sequence of events in the passage of a high voltage current through highly rarefied gases.

Metal Radiography as worked at the Research Dept. at Woolwich. Among other applications, is the estimation of the amount of a heavy element alloyed or mixed with lighter, *e.g.*, the quantity of lead present in different specimens of brass. An ionization method, or a simple electroscope, may be used.—W. J. Wiltshire, Jl. Ra., per J.R.S., Oct., '23, 155.

X-Ray examination of coal, with description of a unit for making examinations.—C. Norman Kemp, J.R.S., Oct., '24, 174.

Treatment of Injuries caused by Electric Currents.

In case of shock—death is only an apparent death at first—it may be possible to resuscitate by artificial respiration if used *at once*. If patient is in contact with the wire pull him away by catching hold of his *clothing* or by using a good thick layer of cloth, *e.g.*, one's coat (*dry*), or by using a newspaper. Do not touch him unprotected—use rubber gloves if available. In any circumstances the breaking of the current means a fresh shock to the individual concerned. If in contact with a live wire this is to be cut, if possible, with long iron scissors in wooden handles.

For Treatment of Burns Boric Acid Compresses or Charcoal Poultices if there is much destruction of tissues. A common result of a severe electric shock is rupture of *fine* vessels in the brain. Hence, in *first aid the head should be raised, not lowered*.

A dry skin offers greater resistance to the entrance of electrical current than a moist one.

100 volts is thought to be dangerous—50 may be considered unsafe. The danger depends also on amperage—1/10 ampere would produce death, but medically persons have 'endured' one ampere without fatal results. The difference in sensibility to electrical current on the part of animals is very great. 100 volts will kill a horse or dog, whilst author had been unable to kill a frog by electrical current.

A current of only 65 volts killed a man through touching an electric lamp; on the other hand there are instances of even 20,000 volts not killing.

Electricity, like poisons, affects in different degree various animals and persons—tortoises in addition to frogs are almost immune, while mice and horses are most susceptible.—Prof. Jellinek, B.M.J. ii./12, 1471.

45 deaths by shocks of less than 250 volts during 10 years, only three deaths from *continuous* current during period.—Scott Ram, B.M.J. ii./12, 1471.

Deaths by Electric Currents, Description of.

There is not the smallest danger of sudden death if the current enters one foot or leg and leaves by the other, but there is danger if only 65 volts travels *through the thorax and so has chance to pass through the substance of the heart*. Account of experiments of electrocution of animals. The frog survives currents of all voltages—1,000 volts and more—and shocks from induction coils and charged Leyden jars. The dog, on the other hand, can be killed with certainty by an alternating current of perhaps 15 volts or 60 m.a. applied so as to pass largely through the heart muscles for 2 seconds only.

The question of danger to man of electric currents is discussed under six headings (a) *Voltage*.—Death has occurred from shock at voltages as low as 65 with *alternating* currents. In one case a *direct* current at 95 volts caused death. (b) *Amperage*.—70 to 90 m.a. of an ordinary alternating current would be enough if the current went through the chest and heart. (c).—*Duration of the contact*. (d).—*Industrial alternating currents* are, other things being equal, more dangerous than continuous currents (2 or 3 times as powerful.—Board of Trade agrees as to this). (Alternating current that reverses the direction of its flow 100 times a second is described as an alternating current of 50 *periods* or cycles a second, or as having a frequency or periodicity of 50 cycles). The frequency is of great importance in considering its dangerousness to life. (e).—*Position of electrodes*. The heart is the danger point. (f).—*Resistance at the Electrodes*.

All cases of electric shock should be treated by *artificial respiration* immediately after the accident.—S. Jellinek, Arch. Radiol., 27, 317.

The best explanation of deaths from electric shock is that they are due to a sensory stimulation causing paralysis of the respiratory centre, justifying artificial respiration. Many cases may be only apparent death, real death supervening from lack of means of carrying on the essential functions of the body.—Bernard Spilsbury, Arch. Radiol., 27, 316.

'Wireless' Head Phone. Death by Electrocutation.—A bare wire in the flex of a standard lamp caused short circuit. Another bare wire in the telephone circuit caused a short circuit in this through the metal body and *wireless head-phone bands*. Owing to the coincidence of these two defects in two separate circuits the lady received the full lighting current through her body, entering by the head-lamp and leaving by the earth of the crystal receiving set. The current was alternating 240 volts.—E. E. Jenkins and W. L. Cowardin, B.M.J., ii./27,98.

Treatment of Persons Struck by Lightning.

Fresh air, loosen clothes, artificial respiration. If it were immediately—within a few minutes—available to give strong electric shocks to the præcordia, it would be worth trying in desperate cases. No stimulants seem to give success.

A most extensive literature on these matters.—A. J. Jex Blake, B.M.J. i./13,423,492,548,601.

Static Electricity, Uses of.

In relief of pain in neuritis, lumbago, and other myalgias, and in synovitis it is effective from its first application.

Lupus treated in a few months by this, which by Finsen method certainly would require two years.—P.R.S.M. Electro-Therap. Sec., Feb. 10,73,84.

For ordinary purposes a machine with 8 or 10 revolving plates is used. The Static Induced Current was praised in America for sciatica. In Morton's method of Static Induction Leyden Jars are connected to the two poles and their outer coatings are attached to connecting cords—ordinary pad electrodes which are applied to skin and muscles. The Static "breeze" or indirect spark application is also used for muscular pains.—B.M.J. ii./11,579.

Lumbago well treated by combined radiant heat and static wave current.—A. P. Luff, B.M.J. ii./13,858,859

Static bath, static wave current, static induced current, brush discharge, static spark, high-potential glass vacuum tube current employed safely in a variety of affections. F. H. Humphris, B.M.J. ii./22,555.

High Frequency Current.

This consists of a condenser discharge through a coil of high self-induction the resulting discharge being of very high rate of oscillation and of high voltage.

D'Arsonval first described the method of applying electric currents of high frequency.

The principle of the apparatus required is simple, *i.e.*, to charge Leyden Jars whose outer coatings are connected by a helix of wire or solenoid. The inner coatings of the jars terminate in knobs whose distance apart can be adjusted to suit the sparking distance of the charging electromotive force. The jars when charged to a sufficiently high potential (from a Wimshurst machine or from an induction coil of large size or through a high potential transformer from the alternate current supply mains) discharge in an oscillatory manner across the air gap and through the solenoid connecting the outer coatings and the latter becomes the seat of electro-magnetic induction effects, comparable to those of the primary circuit of an induction coil, so that a derived circuit formed by wires leading from the two ends of the helix yield a current, as do the wires of the primary current of a coil—the apparatus is in short a modified induction coil.—Lewis Jones.

There are four methods of administration of high-frequency currents:—

(1). Auto-condensations, in which the patient is connected directly to one pole of the high-frequency transformer and lies on a couch, the other pole being a plate under the cushion which acts as an insulator across which the current jumps at each impulse.

(2). Auto-conduction, in which the patient sits inside a cage composed of a solenoid of thick copper wire from which the current is discharged through the patient on all sides.

(3). Effleuve, which is the application of high-frequency currents locally in the form of a brush discharge, *i.e.*, a shower of minute sparks.

(4). Direct application which, as its name applies, is the direct application of electrodes to the body. These electrodes are usually made of glass and shaped to fit various parts of the body, including the cavities.

Uses.—These waves modify the sensibility amounting almost to an anæsthesia. Pruritus, psoriasis, eczema, alopecia, zona, acne, impetigo, neuralgia, ataxy neurasthenia, warty growths, trachoma, lupus vulgaris, rheumatic pains and lupus erythematosus have been treated with good results.

There is an inclination among many neurologists to look somewhat askance at H.F. work. Many neurasthenics—including in that term able-bodied persons merely nervously overtired—frequently find H.F. applications of benefit,—it may, if nothing else, be regarded as a useful tonic.—B.M.J. ii./10, 527, 559.

Effects of Electrical Currents on blood pressure.—Cases of hypertonus in which the motor spasm was relieved by high frequency—in neurotic subjects, chronic Bright's disease, lumbago, sciatica, gouty eczema, acute urticarial kraurosis vulvæ, climacteric flooding.—B.M.J. ii./10, 105.

High frequency in various diseases.—Luke, Pr. June, 1914, 845.

Changes in body temperature and tissue metabolism are produced. Hæmorrhoids, anal fissures, skin affections, asthma and incontinence of urine may be treated.—W. F. Somerville, B.M.J., ii./22, 557.

The treatment of cataract by mild high frequency currents and Violet Rays seemed promising.—C. E. Shelley, Arch. Radiol., 1922, 27, 177.

Diathermic treatment.

For passing heat into the body and for coagulating purposes. A tension of 200 to 800 volts and an amperage up to $2\frac{1}{2}$ amps. are used.

In D'Arsonvalisation high tension, 100,000 to 150,000 volts, is necessary for production of effleuves, fulguration, etc., but at the moment when the human body is introduced in the circuit the resistance is so much increased that the tension falls to 2,000 volts or less and a great part of the energy is transformed into heat.

Nagelschmidt's Apparatus consists of oscillating circuit, condenser, spark gap and self-induction coil giving about 1,500 sparks per second. Diathermic effects extend evenly to a considerable depth. The conductivity for various tissues is almost the same—hence currents can be exactly localised.

Clinically the method is applicable in two ways, (1) by elevating the temperature of the tissue to coagulate and hence destroy, e.g., malignant tumours, (2) to raise temperature only slightly—to stimulate vitality. In the first case diathermy is rarely practised to a greater depth than 1 or 2 Cm., and this is supplemented by scraping. Among the several advantages claimed for the treatment we notice the following:—In operating on a cancer, lupus, etc., it is never certain how often the knife cuts through layers of proliferations of cancerous cells or lymph vessels filled with tubercle. There is always danger of transporting bacilli or cancerous cells into the newly-opened lymph channels. Seals the lymph-channels and blood vessels, and permits extensive operations without bleeding. $2\frac{1}{2}$ amps. usually sufficient.

DERMATOLOGY.—Fulguration is useful and rapid.—W. Knowsley Sibley, Pr., Oct., '21, 246.

MALIGNANT DISEASE.—Malignant new growths, innocent new growths, infective granulomata, and scar tissue treated. Work at Bart's.—E. P. Cumberbatch, B.M.J. ii./21, 275.

The cautery on a large scale can be applied to parts almost inaccessible.—Clayton Green, B.M.J. i./22, 952.

MALIGNANT DISEASE of the tongue, naso-pharynx and cervix uteri, naevi, papillomata of bladder, fungating malignant growths of cutaneous and mucous, cutaneous areas, treated.—C. W. S. Saberton, B.M.J. ii./21, 276. See also F. Howard Humphris, *ibid.* 279.

Malignant disease of mouth, pharynx and nose.—N. Patterson, B.M.J. ii./23, 56. See also Sir W. Milligan, B.M.J., i./26, 367.

GENITO-URINARY WORK.—Papilloma of the bladder. Vesical and ureteral calculi and in gonococcal infections.—K. M. Walker, Pr., Mar., '22/192. See also W. Hill, L.i./14, 1501; ii./14, 385.

Diathermy Treatment.—W. J. Turrell, B.M.J. i./23, 143.

GONOCOCCAL INFECTION treated. Gonococci are destroyed by heat which is not high enough to damage the tissues. Permits of raising the temperature of the tissues *en masse*. In gonococcal arthritis pain abolished in a short

time. Also in gonococcal orchitis and epididymitis.—E. P. Cumberbatch and C. A. Robinson, B.M.J. ii./23,54; ii./25,638. See also B.M.J.E. i./26,65.

Diathermy an effective remedy for gonorrhœal infections in the testis and urethra of males and in the urethra and cervix of females.—B.J.M.i./25,161.

DYSMENORRŒA relieved.—E. P. Cumberbatch, L. ii./23,564.

For HIGH BLOOD PRESSURE, stated to give better results than drugs. Encouraging results in angina pectoris.—E. M. Brockbank, L. ii./23,883.

INTRANASAL LUPUS treated; good results.—W. J. Harrison, B.M.J.i./24,423.

PNEUMONIA AND BRONCHO-PNEUMONIA. Striking results from diathermy in conjunction with Ultra-Violet light.—C. B. Heald, L. i./25,1162.

PROSTATIC OBSTRUCTION.—Should be reserved for the large and small fibrous prostates and the atrophied prostate, where it leads to better functional result and lower mortality than after prostatectomy.—T. E. Hammond, B.M.J. i./26,95.

GRAVE EPISTAXIS.—Electrocoagulation (with the diathermy apparatus) recommended.—Per Jl. A.M.A. ii./25,396.

NON-INFECTIVE ARTHRITIS in women well treated.—E. P. Cumberbatch and C. A. Robinson, B.M.J., i./26,612.

Ulcerative Rontgen or Radium DERMATITIS successfully treated by diathermy. Treatment with Ultra-Violet rays is absolutely contraindicated and even dangerous.—Per Jl. A.M.A. i./29,185.

Alternating Magnetic Fields apparently stimulate the nerves of sight and possibly of hearing.—Prof. Silvanus P. Thomson's Experiments at the City and Guilds Tech. College. The colours and lights were originally seen at night over some of the magnetic machinery by the workmen at the Nitrate Works at Notodden, in Norway.—J.R.S., July, 1912.

Radiant Heat.

Consists in employing the heat and light produced by a number of ordinary incandescent electric lamps within a reflecting case.

Dry hot air produces a local hyperæmia and so relieves painful joints, chronic rheumatism and arthritis. Steam used in addition sometimes.

Finsen Lamp.

The concentrated light produced by this lamp is violet and ultra-violet. It is produced by an arc lamp in which the heat rays are cut off. Finsen's original lamp has been improved, and is now known as the "Finsen-Reyn" lamp.

Injections of fluorescent substances, *e.g.*, *Æsculin* 5 minims of a 5% solution immediately beneath the skin to be treated (*v.*, Vol. I., p. 835), and are sometimes used as adjuvants.

CHRONIC ECZEMA.—100 cases in the Finsen Institute at Copenhagen well treated by the application of concentrated light from a Carbon Arc lamp. Single exposure for each spot 70—140 minutes of a Carbon Arc light of 50 amperes and 55 volts. As it is laborious and expensive, its use should be limited to resistant cases.—Svend Lomholt, per Jl. Trop. Med., June 1/23,202.

In LUPUS and other forms of tuberculosis.—A. Reyn, B.M.J. ii./23,499.

90% of cures obtained in lupus vulgaris and other forms of skin tuberculosis with combined treatment locally and the light bath.—L. ii./23,511.

TUBERCULOUS LARYNGITIS at Copenhagen, 50% of cases arrested.—L. ii./23,512; O. Strandberg, L. ii./23,1237.

Carbon arc-light in lupus. 70% of cures in the dry type at London Hospital by Finsen's method.—J. H. Sequeira, per Jl. Trop. Med., Sept. 15/23,292. Of little use in lupus erythematosus.—B.M.J. ii./24,514.

Bactericidal power of blood diminished after excessive exposure to.—Sir Almroth Wright, C.D., Mar. 17/24,698.

By increasing the present water-filter of 30 Cc. in the Finsen Carbon Arc lamp to 91 Cc., all the infra-red and a good deal of the outer-red rays are absorbed, thus diminishing the heat of the light column by more than 33%, eliminating pain and permitting increase of intensity of irradiation. Therapeutic effect not diminished.—Svend Lomholt, L. i./27,15.

No artificial source of radiation yet found which has a spectral energy distribution exactly like that of sunlight: that of the Carbon Arc is the closest approach, but even that contains Ultra-Violet light of very short wave-lengths and infra-red radiation of long wave-lengths not found in sunlight: it also

emits an intense violet radiation in excess of that in sunlight.—Jl. A.M.A. i./29,836.

Infra-Red Rays have much greater power to penetrate tissues than Ultra-Violet Rays. They cause marked vasodilation, a progressive increase in the number of red corpuscles, marked diminution of leucocytes, and increase in temperature of plasma, and in addition exercise a remarkable analgesic effect. They give rise to intense hyperæmia with redness of skin in zone irradiated, usually persisting for 2 to 3 hours.—B.M.J.E. i./26,26.

'Grenz' or 'Infra-Röntgen' rays, a new form of actinotherapy. The rays are situated between the Ultra-Violet and Röntgen rays and have a wavelength of 1.2 to 2 Angstrom Units. One unit of 'Grenz' rays produces a mild erythema from 12 to 24 hours after exposure: redness disappears in 10 days and dose can be repeated every 2 weeks for several doses. Most diseases require doses of 2 units. Special low tension apparatus ranging between 5,000 and 9,000 volts necessary. Of value in skin diseases.—Per Pres., Oct., '28,321.

Ultra-Violet Rays. (Uviol Light.)

The first form of ultra-violet Light was the Finsen Lamp. The Carbon Bisulphide Lamp and the Mercury Vapour Lamp also produce ultra-violet light; the latter has been developed by P. Cooper Hewitt. Schattner and Kusch enclosed the mercury in tubes of fused rock crystal—thereby obtaining a very strong source of the light. For lighting, these quartz tubes must be enclosed in glass which completely absorbs the 'uviolet' Rays.

A resistance coil enables voltage to be adapted to the requirements of the lamp. The eyes and skin must be protected in using by an ordinary sheet of glass.

Tungsten Arc Light—The amount of ultra-violet radiation obtained from any metallic electrode appears to be directly proportionate to the melting point of the metal. Tungsten has the highest melting point of any metal obtainable. Tungsten arc electrodes appear therefore to be the most efficient source. Radiations have destructive action on micro-organisms and cause active hyperæmia in superficial tissues. Protection of the eyes essential. Indolent and sloughing wounds much benefitted, also pustular eczemas, lupus erythematosus temporarily improved.—W. J. Turrell, L. ii./16,790.

(**Tungsten Syn.** (German) **Wolfram**, $W = 184$. With Uranium and Molybdenum forms the Molybdenum group of metals.

The metal is employed in Coolidge's tube, *q.v.* It is in many respects more durable than platinum and considerably cheaper.)

The so-called "**Simpson**" Light introduced a few years ago was a light of this description in which the electrodes contain Tungsten. It is composed of the rays of the luminous spectrum, together with a large proportion of the ultra-violet. The therapeutic action is due to its richness in ultra-violet rays. The exposures given are short—2 to 5 minutes. Rodent ulcers, lupus, syphilis, eczema and tuberculous glands treated with it at St. Bartholomew's Hospital.

"Titanium Ray."—Experiments show that the penetration of this radiation can be no different from that of other sources with a similar spectral distribution.—B. D. H. Watters, L. ii./28,279.

Effect on Metabolism.—Exposure of the skin of animals to ultra-violet radiation gives increased bactericidal power of the blood and serum, as also do heat rays and mustard poultices! Normal growth can be induced in rats put on a diet deficient in Fat-Soluble Vitamin by irradiating with the

Mercury Vapour Quartz-lamp, provided *wood-sawdust* is present in the jar at time of irradiation and afterwards. **Olive Oil exposed to Sun-light** until bleached kills tubercle bacilli more speedily than Olive Oil not so exposed.—Med. Res. Coun., P.J. i./25,77.

Therapeutic effects of Ultra-violet radiations. *All the benefits are not due to the effect of light—Vitamin A is an important factor.*—C. Lee Pattison, L. ii./24,798.

Ultra-violet light has a distinct effect on cell metabolism, this effect being exerted not only locally on the skin but on deeper organs and the general body metabolism as well.—Jl. Trop. Med., April 1/24,78.

Growth is promoted, it has been said, by breathing air which has been irradiated with ultra-violet light, but Webster and Hill definitely conclude that it has no effect on growth.—Biochem, Jl., 18, Na., 113, '24,761.

Germicidal Effect

Ultra-violet radiation between wave-lengths 2960 and 2100 A.U., is germicidal to bacteria. (The Angstrom Unit is the unit by which wave-lengths are measured, is a length of one ten millionth part of a millimetre, i.e., 10^{-8} Cm.) Rays over this range of wave-length are also particularly absorbed by the substances of which bacteria are composed. Human skin in a layer as thick as 1/10 mm. is practically opaque to radiation over a very similar range.—C. H. Browning and S. Russ, Proc. Roy. Soc. B., Vol. 90, 1917. See also an exhaustive paper by C. A. Schunck.—L. i./17,996.

WATER STERILISATION.—Bacteria in water can be killed with remarkable speed by ultra-violet Rays. The Cooper Hewitt Apparatus provides 132 gallons of sterile water per hour. With a flow of more than 600 cubic metres per 24 hours through the machine, and a consumption of less than 26 Watts per cubic metre, a content of 500 to 1,000 B. Coli per litre and total germs of 20 to 260 germs per cc. in the in-flow: the B. Coli were reduced to nil and the "germs" to practically nil in the out-flow. There would appear to be a wide and great future for this new system. It destroys both pathogenic and non-pathogenic organisms and all spores.

MILK can be sterilised. The proportion of ultra-violet Rays emitted by a Lamp depends on whether it is water-cooled or not, and also upon the age of the lamp. A solution of Ammonium Nitrate under ultra-violet light forms some Nitrite.

Ultra-violet radiation is more intense as the temperature of the tube rises.

Cobra venom is said to be rapidly destroyed by exposure to the rays. Strophanthins have their activity markedly diminished by exposure for 30 to 120 minutes. Saponin completely loses its hæmolyzing power.

Penetrating power of different rays.—Those with wave-length from 2,000 to 2,400 A.U. are stopped in the stratum corneum of the epidermis: from 2,500 to 3,300 are stopped in the stratum mucosum of the epidermis: from 3,400 to 3,900 pass through the epidermis and are stopped by the blood in the subepidermal capillaries. Visible Violet light rays (4,000 A.U.) probably penetrate no further than longest Ultra-Violet light rays, but visible Red rays (7,900 A.U.) may reach the superficial strata of the muscles under the deep fascia. Visible Green and Yellow rays have an intermediate, and invisible heat rays a feeble penetrating power.

Action of various rays on the tissues.—Infra-red rays heat the tissues, but only superficially. Visible light rays also produce heat and with visible Red rays the temperature of the superficial layers of muscle under the deep fascia can be elevated. The 'long' Ultra-Violet rays heat the blood in the subepidermal capillaries but have no action on the epidermis. Rays of wave-length 2,500 to 3,300 A.U. ("medium length") produce chemical changes in the cells of the stratum mucosum, killing the cells, which are cast off by desquamation. The "short" rays (2,000 to 2,400 A.U.) do not produce any biological effect, as they do not penetrate beyond the dead tissue of the epidermis—if they fell on living tissue they would destroy it to a slight depth. Although the rays 2,300 to 2,400 A.U. are the most powerfully bactericidal, they have only very feeble penetrating power. The longer the wave-length the lower the germ-destroying power, and therefore Ultra-Violet rays cannot destroy bacteria by direct action if they be more than the very slightest depth below the surface.

Effect on the skin and body.—The most potent erythema-producing rays are those from 2,900 to 3,000 A.U.: the pigment-producing rays are those from 2,900 to 3,300 A.U. Rays below 2,900 produce marked erythema without pigmentation. Amongst other important effects are the activation of Cholesterol, increase of Calcium and Phosphorus content of blood, and of red blood corpuscles and hæmoglobin, and increased power of the irradiated body to combat infection. It is mainly by indirect action that the rays have therapeutic effect. Only in a very few diseases is local treatment of value and even in these, general treatment is of more value.

Apparatus.—No lamp emits the heat, light, and Ultra-Violet rays of every wave-length. The Carbon Arc lamp emits much heat and light, but the proportion of Ultra-Violet rays is small. Tungsten lamps are poor in heat rays but rich in Ultra-Violet rays. Mercury Vapour lamp the best—rich in Ultra-Violet rays but poor in heat rays: it is a clean cold lamp, working automatically. A full-sized lamp should be used.

Method of exposure.—Patient divested of clothing (except genitalia) and lying on back, eyes protected by goggles, the lamp hanging 3 feet above middle of body, but a little to one side. First exposure 2 minutes front and back, repeated every other day, increasing exposure each time by $\frac{1}{2}$ minute up to 10 minutes each front and back. This completes course. If longer course necessary, save time by bringing lamp to 2 feet and reducing exposure from 10 to 5 minutes. If erythema occurs stop treatment till it has disappeared. In children start with 1 minute exposure increased by $\frac{1}{2}$ minute, and in infants $\frac{1}{2}$ minute, increased by $\frac{1}{2}$ minute.

Diseases and patients in which treatment is likely to produce harmful effects.—Patients with general pyrexia should not receive it. In acute local infection local rays should not be used, nor generally if body temperature is raised. Omit treatment if pus present or suspected. Should not be given in pulmonary tuberculosis except by an expert. Inadvisable in case of failing heart, Bright's disease, and in very old people. Omit during menstruation.—E. P. Cumberbatch, B.M.J. ii./28, 43-46.

There is **no scientific reason to suppose that the supply of Vitamin D to the body is better effected by Ultra-Violet rays than by the direct provision of the necessary food values**, and it costs three or four shillings to give by light an effective supply of Vitamin D that would cost less than a penny if given as Cod Liver Oil. As to the power of light radiations to excite local inflammatory reactions in the skin this can be effected equally as well by a mustard plaster. It would seem to be the duty of those taking the responsibility of prescribing light treatment not only to secure that its known dangers shall be avoided, but to find and announce evidence of its benefits other than those due to commercial advocacy and popular credulity.—Med. Res. Council, Ann. Rept., 1927-28, L. i./29,628. Criticisms of the Report: H. S. Banks, L. i./29,684; M. Weinbren, *ibid.*, 685; G. M. Levick, B.M.J. i./29,620.

The germicidal action of ultra-violet radiation.—B.J.R., Oct., '26,164. Sunlight and artificial sunlight. Influence of on health. Owing to **smoke pollution** in cities, the Ultra-Violet rays are **cut down by half**, and even two-thirds, in comparison with country and seaside places.—L. Hill, B.M.J. ii./25,471.

What any source of Ultra-Violet rays can do is neither more nor less than what the high sun can do at the seaside, or in the clear country air, or in the Alps. A great deal of nonsense talked about different sources and methods of getting Ultra-Violet radiation—it does not signify much what the source is. The active region in the Ultra-Violet spectrum is from 3,200 to 2,400 Angstrom units. The **importance of skyshine**: sky the most valuable source of Ultra-Violet rays. Bright clouds and blue sky give more Ultra-Violet radiation than the high sun and far more than the low sun.—Leonard Hill, B.M.J. i./26,618.

Discussion as to cost of running the plant.—B.M.J. ii./25,495.

The Acetone-Blue Gauge shows that on the average two-thirds of the Ultra-Violet rays are cut off by smoke and dust pollution of the atmosphere in the City of London.—Med. Res. Council Report, 1925-6, L. i./27,508. Ultra-Violet Glass (See also Vita Glass, etc., Vol. I. p. 779).

By measuring the Ultra-Violet intensity from the sky-line at the window-sill and comparing the intensity of illumination at the window-sill with that in the centre of the room it has been found that only $1/120$ of the north sky Ultra-Violet light reaches the middle of the room, *i.e.*, a child would have to sit in this position for 20 hours to receive as much Ultra-Violet light as he would receive from 2 minutes out of doors in the noon sunlight. **Cheaper and more efficient to give children a short noon-day recess than to invest in special window-glass.**—L. ii./28,890.

Experiments at Smethwick for a year on 240 school-children, proved that apart from slight increase in hæmoglobin in children of Vita Glass window classes, the benefit was small, the probable reason being that the children had little of their skin exposed. Open-air schools preferable.—per L.ii./29,398.

Vita Glass exposed to sunlight undergoes slight diminution of transparency to shortest wave lengths for 9 months or less period.—Vita Glass Marketing Board. L. ii./29,690.

A Practical Window for Transmitting U.V. Rays from Sunlight.

A cheap, practical, and effective window for transmitting U.V. Rays may be made from Cellophane. The Cellophane is reinforced by being sandwiched between two layers of coarse chicken wire affixed to a wooden frame (1 to 2 inch mesh wire being used), and will last for a year. The material allows the shortest (curative) light-waves to pass. Glass used for the purpose loses a lot of its transparency by exposure.—A. H. Pfund, JI. A.M.A. ii./28,19.

It strikes us as a very good idea—climate permitting.

A new **Daylight Lamp** for actinotherapy and general illumination—designed to provide a **balance of visible and Ultra-Violet rays** comparable to that of sunlight in relative intensity of radiation and in biological action.—A. Eidenow, B.M.J. i./29,680.

Ultra-Violet light depresses the lipase and stimulates the protease in the blood.—per JI. A.M.A. ii./25,66.

Sale of Ultra-Violet light lamps to the public for self-treatment dangerous and detrimental to public welfare. Firms thus selling or advertising the lamps are banned by the American Medical Association. Need for similar action by other medical bodies.—L. i./27,451.

Dosage in Ultra-Violet treatment—Methods of dosage consist of (1) biological standardisation, using *infusoria*, (2) test of sensitiveness of the skin to light, and (3) effect of a test dose on the bactericidal powers of the blood. The **bleaching** of an **Acetone solution of Methylene Blue** may be used in place of the *infusoria*.—A. Eidenow, L. ii./25,317. See also A. Webster and Co-workers, L. i./24,745.

A note on dosage in Phototherapy.—A. Eidenow, L. ii./26,645.

Chemical method for standardisation—the **Uroxameter**, by action of the rays on a solution of Oxalic Acid and Uranium Acetate.—L. i./27,353.—J. E. Moss and A. W. Knapp, Brit. JI. Actino., '27; B.C.A., '27, A.322.

Pastilles of Chloralformamide and Diphenylamine, though originally white in colour, change to a progressively deepening yellow on exposure to Ultra-Violet light. The pastilles are sensitive to all radiations extending between 3,800 A.U. and 2,300 A.U. The measurement of the tint is carried out with a tintometer. The pastilles are unaffected by diffuse light and do not alter in colour for some hours after exposure.—L. A. Levy and D. W. West, B.J.R., Oct., '26,140.

A method for laboratory control of dosage. Some of the prevailing confusion as to the effects of heliotherapy in tuberculosis might disappear if dosage were accurately determined.—J. R. Farp, JI. A.M.A. i./29,312.

General Notes on Treatment with Ultra-Violet Light.

The need for a Register of qualified electrotherapists.—If the unqualified, unregistered chemist, dentist, and midwife were forbidden by law, the unqualified electrotherapist, who handled therapeutic measures as dangerous as those contained in any chemist's shop, and performed operations as delicate as those of any midwife or dentist, ought to be in the same position.—C. B. Heald, B.M.A. Ann. Meeting, B.M.J. ii./28,207.

Ultra-Violet Rays far from innocuous. Chronic nephritis, arteriosclerosis,

and quiescent tuberculosis adversely affected. The Society of Apothecaries of London, with the B.M.A., to set up a standard of proficiency, and a Register of 'biophysical assistants' ('B.P.A.').—A.H. Burgess, Pres. Address, B.M.A., '29, B.M.J. ii/29,135.

Although actino-therapy cannot fulfil all the claims made for it by its most sanguine exponents, there is a definite set of conditions in which its employment is indicated, and though in skilled hands it may prove valuable, improperly used it may do the gravest mischief. Properly applied, it is an important agent in the AMELIORATION OF RICKETS and SURGICAL TUBERCULOSIS—often producing complete cure—and is of benefit in some NEUROLOGICAL CONDITIONS (*e.g.*, acute anterior poliomyelitis, Bell's palsy, the root pain of tabes dorsalis, and herpes zoster), ANÆMIAS and SKIN DISEASES. But it *may do* definite and irretrievable *harm* in pulmonary tuberculosis, arteriosclerosis, chronic nephritis, quiescent appendicitis, and various forms of neurosis. Early or latent phthisis may flare up into activity. Unfortunately, the treatment has fallen largely into the hands of unqualified practitioners—persons ignorant of electricity, ignorant of the physiological effects of irradiation, and ignorant of medicine. At a representative meeting of the B.M.A. at Cardiff, on July 20th, it was recommended that immediate steps be taken to place this form of treatment under the control of the Medical Profession, inclusion being conditional on abstention of treatment of any patient except under general supervision of a medical practitioner, and that an approved Register be made and suitable courses of training organised. The matter is now in the hands of a Special Committee of the Council.—B.M.J. ii./28,662.

Types of cases likely to benefit by light treatment in a general clinic are (1) tuberculosis of bones, joints, glands of the peritoneum, lupus vulgaris of the skin and mucous membranes; (2) rickets; (3) blood disorders; (4) neurasthenia; (5) some forms of chronic arthritis; (6) B. coli pyelitis.—J. H. Sequeira and W. J. O'Donovan, L.i./25,909.

Gratifying results in furunculosis, eczema, alopecia (especially alopecia areata), onychia, chilblains, Raynaud's disease, psoriasis and pruritus, also in disordered menstruation. Relieves pain in sciatica and lumbago and other forms of fibrositis and neuritis. Its immediate analgesic effect little short of miraculous.—F. H. Humphris, Pr., May, '26,380.

Exorbitant claims should not be allowed (the list of conditions for which they have been recommended numbers 1341).—L. A. Parry, per C.D. ii./27,14.

A list of 27 ailments treated, with the type of treatment recommended, and the author's assessment of value.—C. B. Heald, B.J.M. i./29,94-97.

Affections treated with U. V. Light.

ALOPECIA successfully treated with Ultra-Violet Rays.—Per Pres., Oct., '26,347.

ANALGESIC EFFECT.—Radiant heat and Ultra-Violet light are both powerful.—F. Hernamam-Johnson, Pr., Apl., '26,319.

ASTHMA resistant to all other treatment cured by Ultra-Violet light: three cases quoted. Results probably due to leucocytosis, germicidal action, increased absorption of Calcium and Phosphorus and formation of Vitamin D, increase of Iron in the blood and rise of hæmoglobin in the erythrocytes, and increased secretions of thyroid and adrenalin glands.—A. Bryce, B.M.J. ./27,510. The number of attacks is considerably reduced, but relapses occur in two-thirds of the cases.—B.M.J.E. i./27,54.

Infantile asthma well treated. Caution needed owing to production of Ozone by Quartz Lamp with irritant effect on bronchi and lungs.—B.M.J.E. ./26,52.

EYE AFFECTIONS.—Ocular tuberculosis in any form gives ready response Phlyctenular ophthalmia also well treated. Infective irido-cyclitis cases show less dramatic response.—W. Stewart Duke-Elder, B.M.J. i./26,891.

FRACTURES.—Especially where there is delay in union, a combination of J.V. light with direct current proved effective.—C. B. Heald, L.i./25,1162.

HERPES, occurring 5 weeks after a course of Auremetine and Stovarsol, cleared up with no scarring after treatment with Ultra-Violet light—5 minutes

at 2 ft. with the air-cooled Hanovia lamp on four successive days. In a control case not so treated the vesicles and itching persisted for three weeks.—M. Weinbren, L. ii./27,865.

IMPETIGO CONTAGIOSA.—Slight but definite curative effect. General exposure in this complaint safer and more efficient than local exposure at short range.—J. B. Ellison, L. i./27,1345.

LUPUS has been treated.

NASAL and ORAL CONDITIONS—effective.—C. R. Brooke, Med. Jl. and Rec., Dec. 2, '25, 681, per Pres., Feb., '26, 74.

NEURALGIA following herpes zoster well treated with Ultra-Violet Rays.—Raggi Ultravioletti, June, '25, 176, per Pres., April, '26, 138.

NIPPLES, CRACKED well treated with Ultra-Violet Rays, exposures every second day, beginning with 2 minutes, increasing by 2 minutes up to 10.—Bull. de l'Acad. Med., July 21, '25, 828, per Pres., Jan., '26, 47.

NOSE AND THROAT diseases treated.—A. Eidenow, B.M.J. i./29,289.

Tuberculous and other buccal pyogenic chronic ulceration, rapid healing.—A. Eidenow, L. ii./29,651.

PARALYSIS, INFANTILE.—Good results with light treatment in conjunction with local treatment of the affected muscles by Red Rays.—G. Murray Levick, L. i./25,686.

PSORIASIS of 27 years' standing cured by a series of exposures to an air-cooled Mercury-Vapour Lamp.—R. W. MacKenna, B.M.A. Ann. Meeting, 1926; L. ii./26,550. Other speakers were not agreed as to its value.—*Ibid.*

The combined treatment of psoriasis with crude Coal Tar ointment and exposure to Ultra-Violet Quartz Lamp better than either treatment alone. The ointment is applied to patches for 24 hours and removed with Olive Oil. The light is applied for one minute at a distance of 30 inches, and the time increased one minute daily for 3 or 4 days.—per Jl. A.M.A. ii./25,226.

PYORRHOEA with systemic infection. Erythema dose of Ultra-Violet Rays administered to trunk, a specific cure.—B.M.J.E. ii./26,101.

Beneficial results by use, in conjunction with Ultra-Violet Rays, of 1% Eosin in pyorrhœa alveolaris, of 5% Protargol in skin diseases, and of saline in tuberculosis and rickets.—G. Matteucci, "The Limitations and Defects of Actino-Therapy."

RHEUMATIC DISEASE (chronic).—Beneficial. Local analgesic powers considerable in neuritis, fibrositis and arthritis.—A. G. Watson, Pres., Nov., '26, 412.

RICKETS.—The Rays the most active and most powerful treatment in early childhood.—B.M.J.E. i./25,8. See also F. H. Humphris, L. i./25,912.

Rickets treated with artificial sunlight reinforced by administration of Eosin.—Jl. A.M.A., May 1, '26, 1407. 1 grain doses have been used.—W. H. M.

Some recent advances in our knowledge of rickets and allied diseases.—L. G. Parsons, L. ii./28,433-438.

TUBERCULOSIS.—A valuable adjunct to other treatment.—H. Godde, L. ii./23,238. Whole body exposed gradually to the light from short flame carbon arc lamps consuming 75 amps. For patients who are receiving maximum dosage of 2 or 2½ hours it is not economical.—G. B. Dixon, B.M.J. ii./25,473.

Review of treatment of peritoneal and glandular tuberculosis in children by ultra-violet rays during last few years. The authors conclude that (1) the sole use of ultra-violet rays has been of decided value in peritoneal, glandular and osseous tuberculosis, (2) mesenteric glandular tuberculosis is the most rapidly improved, then mediastinal and lastly peripheral glandular tuberculosis, (3) pulmonary miliary tuberculosis, even in early stage, is unaffected.—B.M.J.E. i./25,3.

Intestinal tuberculosis—relief of symptoms.—Am. Rev. Tub., Sept., '25, per Jl. A.M.A. ii./25,1583.

All forms of tuberculosis, except pulmonary and meningococcal, in which it is contraindicated, are benefited—fresh air an important adjunct.—Can. Med. Assn. Jl., per Jl. A.M.A. ii./25,1091.

The original idea that artificial heliotherapy would prove an almost specific treatment for surgical tuberculosis has not been justified. A series of cases

thus treated showed no marked improvement over those not so treated. Artificial heliotherapy does not change the fundamental principles of treatment of surgical tuberculosis.—E. C. Mekie, B.M.J. ii./28,243.

Results in pulmonary tuberculosis not likely to be spectacular, and omission not necessarily detrimental to the patient's best interests.—per JI.A.M.A. i./28,426.

Genito-urinary tuberculosis: of value.—Treatment lasts for 2 years.—B.M.J.E. i./25,12.

WELFARE WORK, light treatment in—children in Islington.—D. C. Colebrook, B.M.J. ii./25,475.

No practical value as a prophylactic against acute or chronic radiodermatitis and a combination of Ultra-Violet Ray and Roentgen Ray is more likely to be followed by sequelæ than with Roentgen Ray alone. Actinotherapy is of some value in the treatment of chronic ulcers and telangiectasia caused by Roentgen Rays or Radium.—G. M. MacKee & G. C. Andrews, JI. A.M.A. ii./25,1719.

Deleterious Effects.

Severe dermatitis following an artificial sun bath from electrical lamp.—H. MacCormac and H. M. McCrea, B.M.J. i./25,693.

Patients with unduly *low blood pressure* may be intolerant to ordinary doses and develop lassitude, depression, headache, etc., but will often receive benefit from subminimal doses.—J. B. Ferguson, B.M.J. i./26,403.

Skin irritation following. In the milder cases bathing the skin with alkaline lotions is effective. A routine examination of the urine is now undertaken and in cases showing marked acidity an alkaline mixture is given, and increased exercise in the open air, to prevent irritation which may arise from deficient alkaline reserve.—S. van S. Boyd, L. ii./28,1076.

Erythema appears to be caused by the same mechanism by which mustard and other skin irritants act. A non-bactericidal, fluorescent substance may be rendered bactericidal by influence of light. Sunshine is not a universal panacea in disease, and in health *most of us take some pains to avoid it*—on occasion.—W. E. Dixon, B.M.J. ii./25,499.

Minimum quantities of *heavy metals* circulating in the blood considerably increase effect of Ultra-Violet rays on the organism, and *vice versa* the efficacy of heavy metals is increased under influence of Ultra-Violet light.—Max Ostermann, "Ars Medici," Vienna, Vol. 3, No. 3, Mar., '25.

By exposure of mice to Ultra-Violet rays for 8 months *papillomas* and *malignant epitheliomas* of the skin were produced. Mice tarred for one month failed to develop cancer, but when tarred and exposed to Ultra-Violet rays for one month three mice developed growths.—G. M. Findlay, L. ii./28,1070.

External treatment of painful affections, *e.g.*, polyarthritis and neuralgia, by compresses of *irradiated oil*. The fresh oil (sunflower, peach, nut, or cod liver), is exposed to 500, 1,000, or 1,500 Ultra-Violet units. Conspicuous reduction of painfulness and diminution of local heat. The activity of the oils lasts 15 months.—Th. Rothstein, Congress of Radiol., Stockholm, July, '28, L. ii./28,353.

'The Quartz Mercury Vapour Lamp'—a useful book on.—J. Bell Ferguson, B.M.J. ii./26,1058.

Sugar Synthesis.—Prof. Baly of Liverpool University, and his Co-workers, succeeded in producing sugars by the action of Ultra-Violet light on solutions of Carbon Dioxide, in which Nickel Carbonate was suspended. The essential feature in the leaf is the existence of a surface on which the synthesis can take place—a *coloured surface* is essential. The chemistry of life would seem to be one of high energy while that of man's endeavour is the chemistry of low energy.—P. J. i./28,120.

Reflected Sunlight.

Laryngeal tuberculosis has been treated by the sun's rays reflected from a laryngoscopic mirror, but the evidence of its value is doubted.

B. typhosus is rapidly killed by sunlight. In an experiment in India 240,000 organisms were reduced to *nil* in 2 hours.—R. T. Hewlett.

The value of sunlight.—B.M.J. i./14,210.

Bactericidal action of light.—Annual Report of the Com. of the Privy Council for Medical Research, 1922-3.

SUN CURE OF TUBERCULOSIS. From the sea at Hayling it seems that the medicinal rays are reflected with high efficiency. Patients for particular exposures derive enhanced advantage.—Sir C. Allbutt, B.M.J. ii./23,111.

Good effects from the sun cure of tuberculosis can only be obtained by means of exact medical observation and supervision. The patient should be slowly acclimatized to the sunshine, starting with 5 minutes exposure with the legs only, and slowly increasing daily until in 12 days a complete sun-bath of an hour's duration is allowed. Results of treatment remarkably good. In unfavourable weather artificial sunlight is given.—L. ii./23,237.

The only untoward result seen in light bath treatment is the occasional "flare up" of a tubercular process, especially where there is pyrexia. Wise to begin treatment of visceral tuberculosis with very short exposures limited to small areas. It is generally accepted that patients whose skin pigments best make the most rapid and complete recoveries, though the pigmentation is probably only an index of some chemical change in the blood.—J. H. Sequeira, B.M.J. ii./24,515.

When undertaken not under medical advice, insolation is suitable for the well man only who feels the better for it. For the sick and infirm it should never, under any circumstances, be undertaken except under medical supervision. The Sun Cure should be regarded merely as an adjuvant method in non-pulmonary tuberculosis. While advocating the treatment, the author utters a warning that it must be wisely and carefully employed—gradual exposures are essential.—Sir H. J. Gauvain, B.M.J. ii./24,234.

The dangers of misapplied sun-cures.—Lennox Wainwright, Pr., Sept. '24,197.

The treatment of chronic arthritis by heat and light. The bodily temperature cannot be raised beyond a certain degree without inflicting injury. In any doubtful case of ARTHRITIS the following precautions should be observed in ordering hot air, radiant heat, and light baths:—the full bath should be used in preference to a local bath; temperature should not be more than 150° F. at commencement of the course, gradually increased, if necessary; ventilation should be free; bath should not exceed 15 to 20 minutes duration.—A. G. Dampier-Bennett, Pr., Dec. '24,426.

Moonlight may be responsible for decay. Being reflected light it is more or less polarised, and possibly polarised light may exert peculiar chemical action. Experiments on slices of cut fish with polarised light and direct light respectively showed that the former always decomposed first.—Chemical News, per L.ii./13,1203.

RADIUM.

$Ra=225\cdot95$

Radium was prepared by Madame Curie and M. A. Debierne (1910) in the pure basic condition by electrolysing a solution of a Radium Salt, using a Mercury cathode:—

Preliminary experiments were made with Barium, using about 0.1 Gm. of material, by Guntz's method. The amalgam was obtained by electrolysis of a solution of 0.106 Gm. of pure Radium Chloride with cathode of mercury (10 Gm.) and anode of Platinum Iridium. After electrolysis, the solution contained 0.0085 Gm. of the salt. The dried amalgam was heated cautiously in a quartz tube in a current of pure hydrogen, purified by passage through the walls of a Platinum tube heated in an electric furnace. Most of the mercury was distilled at 270°. At 400° the amalgam became solid, and its M. Pt. rose progressively as the mercury was driven off to 700°, when no more mercury volatilised, but the Radium began to volatilise and to attack the quartz tube. The boat now contained a brilliant white metal, fusing about 700°, which was considered to be pure Radium. It adhered to the iron, and blackened on exposure to the air, probably forming the nitride. A particle falling on white paper produced a blackening analogous to a burn. The metal decomposed water energetically, and dissolved for the most part. The small, black residue

(? nitride) dissolved completely in a very little Hydrochloric Acid, showing that no Mercury was present. The penetrating rays from the boat containing the metal, sealed in a glass tube, showed the normal increase following the law of production of the emanation.

Becquerel in 1896 commenced the experiments which led up to M. and Mme. Curie's discovery of Radium by finding accidentally the radio-activity of Uranium-Potassium Sulphate.

A photographic plate in Becquerel's hands was affected by the Uranium compound through a sheet of copper in the dark without any previous "lighting" being necessary to produce fluorescence. Whilst Uranium will fog a photographic plate in some hours, Radium will produce a like effect in a few seconds. The radio-active energy of Radium may be taken to be about 2 million times that of Uranium.

M. and Mme. Curie concluded that there must be present in Pitchblende an element many times more radio-active than Uranium. On analysing Pitchblende it was found that the acid group precipitate (containing Bismuth with Polonium) had considerable, but the alkaline earth group (containing Radium) the greatest, activity.

The 25th Anniversary of the discovery of Radium by M. Pierre Curie and Mme. Curie was celebrated at the Sorbonne on Dec. 26, 1923. A Bill passed by the French Government grants Mme. Curie a pension of 40,000 francs a year. (M. Curie was killed in an accident in the street in Paris several years ago).

The commerce of Radium.

From time to time various Pitchblende and other Uranium-containing Ores have been mentioned as being worth operating for Radium both in this country (Cornwall) and abroad, *e.g.*, it is stated that at present about 95% of the world's output comes from the Uranium Ore deposits in the Belgian Congo (Haut Katanga). Uranium Ores occur at that locality in conjunction with copper. The ore is conveyed first to Beira and thence to Oolen in Belgium for working.

The American and other factories are in a state of partially suspended animation, unable to compete with the Belgians.

The Radium salt chiefly in request now is the Sulphate which is most suitable for the preparation of Radium Applicators, the Chloride and Bromide being preferable for emanation purposes. The price of Radium rose from £2 to £5 in 1904 to £12 in 1906, £27 in 1910, £30 in 1912, and £36 in 1914: by 1922 it had dropped to £22 per milligramme, with a further fall to £14 in 1923, the price now being £11 10s. *To the end of 1924 a little over 300 Gm. of Radium had been produced*, of which 120 Gm. are owned by America. The output of Radium is being kept under control in order that the supplies may not be increased beyond the demand.—B.J.R., Oct. '28, 390.

Carnotite, which contains Uranium and Vanadium, from America and Australia and **Autunite** from Portugal and China are sources of supply, also **Torbenite** but these minerals are by no means so rich in Radium. Carnotite usually contains the equivalent of about 10 mgr. $\text{RaBr}_2 \cdot 2\text{H}_2\text{O}$ per ton.

Autunite (from Portugal) is comparatively rich in Uranium but much contaminated with soil. The ore contains from 1 to 1½% of Uranium and from one ton of such material about 2 milligrammes of Radium Bromide can be produced.

A lode containing Pitchblende found on the Kingswood Estate, Buckfastleigh, S. Devon. Uranium Oxide content 26%.—J.R.S., Apl. '19, p. 28.

TOLGARRICK MINE near Truro contains mineral rich in Uranium; to be re-worked.—L. i./22, 260.

Euxenite, a radioactive mineral in the state of Minas Gerses, Brazil, to be worked for Radium.—L. i./22,260.

The British Radium Corporation deal with Pitchblende at Trentwith in Cornwall, but have extracted probably not more than 10 Gm. of Radium.—W. E. Dixon, B.M.J. i./29,238.

The Government of Australia has purchased 10 Gm. of Radium at a cost of £100,000, 2 Gm. having been allotted to Sydney, 2 Gm. to Melbourne, and 0.5 Gm. each to Brisbane, Adelaide, Perth, and Hobart, 4 Gm. being kept in reserve.—per J.L.A.M.A. ii./28,1050.

Hydrated Radium Bromide $\text{RaBr}_2 \cdot 2\text{H}_2\text{O} = 421.814$, occurs in hard, yellowish, crystalline particles, and is best kept in hermetically-sealed containers so as to exclude moisture, for reason explained later.

Yield of Radium.

Upwards of 0.25 Gm. of pure Radium Bromide can be obtained from a ton of Pitchblende residues. This approximates statements one finds elsewhere to the effect that Pitchblende contains 1 of Radium in 5 million parts or an ounce in 150 tons. Other minerals yield considerably less.

A CHEAP AND RAPID METHOD OF EXTRACTION FROM PITCHBLENDE.—100 kg. of finely ground Pitchblende with 400 kg. concentrated crude sulphuric acid are heated for several hours. The mixture is then boiled with from 10 to 20 times the quantity of water, left to stand, decanted and the residue washed with water and the liquid filtered off. The dry residue (about 45–50 Kg.) is heated with 140 Kg. of commercial caustic soda in an iron crucible till a uniform mass is obtained, *i.e.*, in about 1 to 2 hours. This is afterwards boiled several times with about 1,000 litres of water, left to stand, decanted and filtered. The moist residue is then boiled with 5 Kg. of 20% sulphuric acid solution, filtered and washed with water. Raw sulphates of Radium to the amount of 0.5 Kg. are thus obtained,—these can be quickly converted to chlorides by melting with alkaline carbonates, washing thoroughly with water and dissolving the residue in pure hydrochloric acid.—P.J. ii./10, 453.

Characters of Radium.

Radium should be placed below Barium in the Mendeléeff series, and on the same line as Thorium and Uranium (*vide Periodic Table*). These three radio-active elements have the highest atomic weights. Radium is divalent. Its spectrum resembles those of the alkaline earths. A freshly-prepared Radium Salt has its energy stored up and reaches its highest power in three weeks or so. The element is assumed to contain normal atoms and these in succession become the radio-active ones. Radium and its disintegration products emit rays which will be described. See 'Atomic Disintegration.' Radium decomposes water into hydrogen and oxygen. Oxygen is converted into ozone. It turns glass in its proximity to a violet colour. Mercury is converted into the yellow oxide.

The rays emitted burn the skin if kept in close proximity for a length of time.

Electrical Properties of Radium.

The rays emitted by a highly active preparation discharge a charged gold-leaf electroscope even through an inch or more of iron or zinc—5 milligrammes will do this at a distance of a few yards.

This occurs whether the charge on the leaves be + or –. All the three types of radiation from Radium have the effect of ionising air in the electroscope, breaking the molecules into constituent atoms, each of which is electrically charged + or –. These charged atoms collide with the charged gold

leaves, and such as are of opposite sign to the charge on the leaves neutralise a corresponding amount of electricity on the leaves. One three thousand millionth of a grain of Radium is recognisable by an electroscope.—Soddy.

Tests for Purity.

Good Radium Bromide should light up a screen through several copper coins. It should make Willemite fluoresce. Glew's instrument for estimation of activity consists of an electroscope with ground glass front. A positive charge is given to the leaf by means of a charged camel's hair brush. The time this charge will remain (usually a day or two) is noted. Markings are made on the ground glass at certain intervals, and on bringing a known weight of pure Radium Bromide, preferably in a metal box, to within a distance of a yard, the time taken for the leaves to fall is observed. Then if a pure sample causes the drop in sixty seconds it follows that the same weight of another specimen doing the same work in 120 seconds is only 50% pure, and so on. In this method the β and γ rays are not measured directly (the α rays do not come in at all) as they do not penetrate the metal box.

A Balance Method for comparing Quantities of Radium.

In making comparisons the best method is to compare the γ -ray activities of the two specimens. If the radium is enclosed in a sealed tube, the γ -ray activity reaches a practical maximum after two months, and the intensity of the penetrating γ -rays emitted serves as a definite measure of the quantity of radium. The greater part of the γ -rays are emitted by radium C., and investigations by Moseley and Makower have shown that about 11.5% of the total γ -ray activity is to be ascribed to radium B. The γ -rays from the latter are on the average much less penetrating than those from radium C., and are completely absorbed by a lead screen 2 cm. thick.

The specimens must contain **no Mesothorium or Radiothorium**. Both the latter substances emit γ -rays of about the same penetrating power as those given out by radium. Since meso-thorium and radium are always isolated together, and are chemically closely allied, it is impossible to isolate pure radium compounds from minerals containing both uranium and thorium. The uraninite deposits at Joachimsthal contain only a trace of thorium, so that the radium from this ore can be obtained practically free from meso-thorium. The electroscope used is surrounded by lead 3 m.m. thick.

The primary β -rays are completely stopped by the lead and the ionisation in the electroscope is due to the more penetrating γ -rays and to the β -radiation to which they give rise. The rate of movement of the gold leaf of the electroscope between two fixed points is proportional to the intensity of the γ -radiation.—Rutherford & Chadwick, J.R.S. July, 1912.

Radium Standard (International).

This consists of 21.99 milligramme of Radium Chloride made by Madame Curie in a thin sealed glass tube at the Bureau des Poids et Mesures at Sèvres, Paris. Another International Standard is kept at the Academy of Sciences at Vienna. Duplicate standards are in the hands of Governments of other countries.

The **British Radium Standard** is kept at the National Physical Laboratory, Teddington. It contains about 20 mgr. of pure Radium Chloride. This Laboratory expresses the activity of specimens submitted in terms of **Metallic Radium** instead of Bromide. *This is preferable to prevent misunderstanding regarding the $2H_2O$ in crystallised Radium Bromide.*

Standard Solution of Radium.—Sealed tubes are made containing 1/100,000 mgr. Radium as metal in 10 Cc.

In estimating radium in samples of its salts, it is necessary to weigh out a small specimen. The specimen should be dissolved in 100 Cc. of water, some pure hydrochloric acid being added; of this 5 Cc. should be diluted to 1 litre, making 1 milligram in 20,000 of water, or 1/20,000th of a milligram in 1 Cc. If 1 Cc. be diluted to 50 Cc. the strength will be approximately that required

for the electroscope, and a comparison may be made with the standard. To calculate the radium to pure crystallised bromide multiply by the factor—

$$\frac{421.814}{225.95} = 1.867.$$

The Katanga Company states their preparations are 98 to 99.5% pure—the highest practicable degree of purity obtainable.

For suggested Standard for the Emanation *vide* Emanation.

Atomic Disintegration.

Radium passes in its change through a series of other bodies.

Uranium and Thorium, according to Rutherford, represent the sole survivals to-day of types of elements common when atoms now composing the earth were in course of formation. Owing to their slow rate of transformation some atoms of Uranium and Thorium have survived—they have not yet completed the cycle of changes which the atoms of other elements have long since passed through.—J.R.S., Oct., '23.

“Any one radio-element like Radium considered any instant among its hosts of atoms, most of which are destined to last for hundreds, or thousands of years, a comparatively very small proportion fly apart every second expelling α particles and becoming emanation atoms. Next second a fresh set disintegrates, and so on, α particles being expelled, and yet so small a fraction of the whole changing that the main part of the Radium remains unchanged even after hundreds of years.”—Soddy.

In the case of the emanation atoms a much larger fraction change per second, producing more α particles, and the active deposit.

The ‘Radio-Active Constant’ λ represents the fraction of the total of an element changing per second. For the Emanation $\lambda = \frac{1}{550000}$. (Rutherford gives 2.085×10^{-6} (seconds) $^{-1}$).

The Average Life of an atom, *i.e.*, the time in seconds it exists on the average before its time comes to disintegrate, is the reciprocal $1/\lambda$. In the case of Radium Emanation the average life is obviously 500,000 seconds, or 5.7 days. (Current figure says 5.55 days).

The Average Life of Radium is probably about 2,600 years. (Current figures state 2,440 years). In other words $\frac{1}{2600}$ part of a given mass of Radium changes annually.

The genetic relation between Uranium and Radium has been established. There is always a definite proportion of Radium to Uranium present in Uranium minerals,—for every 1 part of Radium there always exist 3,000,000 parts of Uranium. $1/\lambda$ for Uranium is 8,000,000,000 years (current figure gives 6.75×10^9 *i.e.* 6,750,000,000 years). The average life is always 1.443 times the time T known as the *period* required for the quantity of the element to be diminished to $\frac{1}{2}$ value. Thus the $\frac{1}{2}$ value of Radium is 1,690 years and $1,690 \times 1.443 = 2,440$ years, *i.e.*, the average life of Radium. For the emanation the average life $= 3.85$ days $\times 1.443 = 5.55$ days.

Conversely to find the ‘Periods’ or ‘Half Values’ from the average lives multiply the average lives by $\frac{1.000}{1.443}$, *e.g.*, the half value of

$$\text{Radium 'B'} = \frac{38.7 \times 1000}{1443} = 26.8 \text{ minutes approx.}$$

It is believed that 1 atom of a radio-active body expels 1 α particle only at each disintegration.

INTERNATIONAL TABLE OF THE RADIOACTIVE ELEMENTS AND THEIR CONSTANTS (1923).

λ (sec)⁻¹ is the *radioactive constant* of the equations of transformation:

$$dQ = -\lambda Q dt, \quad Q = Q_0 e^{-\lambda t}, \quad \log_{10} \frac{Q_0}{Q} = 0.4343 \lambda t.$$

in which Q_0 is the initial quantity and Q the quantity remaining after a time t (seconds).

$\lambda = \frac{dQ}{Q} \frac{1}{dt}$ represents the fraction of the element transformed, reduced to the unit of time.

In the case of a double transformation, the values between brackets [] refer to the constants corresponding with the separate branches; the constant for both branches not being put between brackets.

The sign (?) indicates that the value has been indirectly deduced from the range of the α -rays expelled.

$\theta = \frac{1}{\lambda}$ is the *average life* of the radioactive atoms.

T is the *period*, i.e. the time in which the quantity of radioelement is diminished to one half:

$$\lambda T = -\log_e 0.5 = 0.69315 \text{ and } \theta = 1.443 T$$

Radiation. The brackets () indicate that the radiation is relatively feeble.

a_0 is the *range* in cm. of the α -rays in air at 0° C. and a pressure of 760 mm. of mercury.

The range at $\tau^\circ\text{C}$ and under p mm of mercury is

$$a = \frac{a_0 (273 + \tau) 760}{273 p}$$

V is the velocity of α or β -rays relatively to that of light.

To convert to cm per sec. multiply by 3×10^{10} .

For the α -rays:

$$V = 0.0342 a^{1/3}$$

β_{Al} is the *absorption coefficient* of the β -rays in aluminium, the thickness being measured in cm.

$\mu_\gamma \text{Al}$ and $\mu_\gamma \text{Pb}$ are the absorption coefficients of the γ -rays in aluminium and lead respectively, the thickness being measured in cm.; the latter is only given for the most penetrating type of γ -rays.

If I_0 is the initial intensity and I the intensity after the rays have traversed x cm of the absorbent:

$$I = I_0 e^{-\mu x} \quad \log_{10} \frac{I_0}{I} = 0.4343 \mu x$$

If D is the thickness corresponding with the absorption of one half of the rays:

$$\mu D = 0.693$$

T	$\theta = \frac{1}{\lambda}$	λ (sec.) ⁻¹	Name	Symbol	Atom WT.
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SERIES of URANIUM

4.67 × 10 ³ yrs.	6.75 × 10 ³ yrs.	4.7 × 10 ⁻¹⁸	Uranium I	UI	238
24.6 days	35.5 days	3.26 × 10 ⁻⁷	Uranium X ₁	UX ₁	234
1.15 mins.	1.65 mins.	0.010	Uranium X ₂	UX ₂	234
2 × 10 ⁶ yrs.	3 × 10 ⁶ yrs.	10 ⁻¹⁴ (?)	Uranium II	UII	234
6.9 × 10 ⁴ yrs.	10 ⁶ yrs.	3.2 × 10 ⁻¹³	Ionium	Io	230
1690 yrs.	2440 yrs.	1.30 × 10 ⁻¹¹	Radium	Ra	226
3.85 days	5.55 days	2.085 × 10 ⁻⁶	Radon	Rn	222
3.0 mins.	4.32 mins.	3.85 × 10 ⁻³	Radium A	RaA	218
26.8 mins.	38.7 mins.	4.30 × 10 ⁻⁴	Radium B	RaB	214
19.5 mins.	28.1 mins.	5.92 × 10 ⁻⁴	Radium C —	RaC	214
10 ⁻⁶ sec.	10 ⁻⁶ sec.	10 ⁶ (?)	Radium C'	RaC'	214
16.5 yrs.	23.8 yrs.	1.33 × 10 ⁻⁹	Radium D	RaD	210
5.0 days	7.2 days	1.61 × 10 ⁻⁶	Radium E	RaE	210
136 days	196 days	5.90 × 10 ⁻⁸	Radium F (Polonium)	RaF (Po)	210
.....	Radium Ω' Lead	RaΩ' Pb ²⁰⁶	206
.....	[1.8 × 10 ⁻⁷]	Radium C —	RaC	214
1.4 mins.	2.0 mins.	8.3 × 10 ⁻³	Radium C''	RaC''	210
.....	Radium Ω'' (hypothetical)	RaΩ''	210

SERIES

.....	Uranium ?	?
1.04 days	1.5 days	7.8 × 10 ⁻⁶	Uranium Y	UY	?
1.2 × 10 ⁴ yrs.	1.7 × 10 ⁴ yrs.	1.9 × 10 ⁻¹²	Protoactinium	Pa	?
20 yrs.	28.8 yrs.	1.1 × 10 ⁻⁹	Actinium	Ac	?
19.5 days	28.1 days	4.11 × 10 ⁻⁷	Radioactinium	RdAc	?
11.4 days	16.4 days	7.06 × 10 ⁻⁷	Actinium X	AcX	?
3.9 secs.	5.6 secs.	0.178	Actinon	An	?
2.0 × 10 ⁻³ sec	2.9 × 10 ⁻³ sec.	345	Actinium A	AcA	?
36.1 mins.	52.1 mins.	3.2 × 10 ⁻⁴	Actinium B	AcB	?
2.15 mins.	3.10 mins.	5.37 × 10 ⁻³	Actinium C	AcC	?
4.71 mins.	6.83 mins.	2.44 × 10 ⁻³	Actinium C''	AcC''	?
.....	Actinium Ω'' (hypothetical)	AcΩ''	?

[illegible]

ACTINIUM

U	α	7
Th	β	About 300
Pa	α	3.314	0.0510	8, 9
Ac	—
Th	α (β)	4.36	$\left\{ \begin{array}{l} \alpha 0.0559; \beta 0.38; \\ 0.43; 0.49; \\ 0.53; 0.60; \\ 0.67; 0.73 \end{array} \right\}$	About 170	25; 0.19
Ra	α	4.17	0.0550
Rn	α	5.40	0.0600	10
Po	α	6.16	0.0627
Pb	(β and γ)	Very large	120; 31; 0.45	11
Bi	α	5.12	0.0589
Tl	β and γ	28.5	0.198	$\left\{ \begin{array}{l} 1.2 \\ \text{to} \\ 1.8 \end{array} \right\}$
Pb	12

REMARKS CONCERNING THE NOMENCLATURE IN THE INTERNATIONAL TABLE.

It is desirable that the nomenclature adopted by the International Commission should be accepted universally but that now put forward for the present year is provisional, to serve as a basis of discussion with the view to the adoption ultimately of a standard nomenclature.

The most important points are :

1° The three radioactive emanations have been given the names radon, actinon, and thoron, with the symbols Rn, An, Tn, to suggest both their origin and their chemical character as members of the family of the rare gases of which the valency is zero;

2° In the branches which occur at the C members the sign (') has been used to indicate the products resulting from the emission of β -rays (isotopes of polonium) and the sign (") to indicate the products resulting from the emission of α -rays (isotopes of thallium);

3° The ultimate products have been indicated by the letter Ω .

EXPLANATION OF THE NOTES.

Note 1. *Uranium I.* The value given for θ is that obtained from the equation :

$$\theta = \frac{1}{\lambda} = 2440 \times 0.97 \times 3 \times 10^8 \times \frac{226}{238} = 6.75 \times 10^9$$

in which the number 2440 represents the average life of radium in years, the number 0.97 the branching coefficient and $3 \times 10^8 \times \frac{226}{238}$ is the ratio between the numbers of atoms of uranium and radium in equilibrium in minerals.

If the actinium series is independent from that of uranium I, λ cannot be calculated by this method.

The value of λ obtained by the direct counting of the α -particles from a compound of uranium is 4.57×10^{-18} from which $\theta = 7 \times 10^9$ years and $T = 4.8 \times 10^9$ years.

Note 2. *Uranium X₂* is also called brevium.

Note 3. Radon replaces the names *radium emanation* and *niton* (the latter of which was proposed by Sir William Ramsay).

Note 4. *Radium C* undergoes a double disintegration : 99.97% of the atoms emit β -rays and produce the substance RaC' which gives α -rays, and 0.03% of the atoms emit α -rays and produce the substance RaC'' which gives β -rays.

Note 5. *Radium D* is also called radiollead.

Note 6. *Radium C''* is also called radium C₂.

Note 7. *Uranium Y* is the first known member of the actinium series. It may be derived from Uranium I or Uranium II. In this case, 3% of the atoms of Uranium produce the actinium family, and 97% the radium family.

The hypothesis has also been put forward that the actinium series may be produced independently from a third (hypothetical) isotope of Uranium for which the name actinouranium has been proposed.

Note 8. *Protoactinium* is also called eka-tantalum.

Note 9. A new radioactive substance named uranium Z, and isotopic with protoactinium, accompanies uranium in minute quantity. (*Berichte* : 1921, 54 (B), 1131). Its period is from 6 to 7 hours. It emits a β -radiation for which DAI varies from : 0.0014 to 0.012. Its parent is an isotope of thorium, but it cannot yet be placed in the series.

Note 10. *Actinon* is also called the actinium emanation.

Note 11. *Actinium C.* 0.2% of the α -rays emitted by this substance have a range $a_0 = 6.10$, instead of 5.12. From this it has been concluded that 0.2% of the atoms undergo a transformation by the emission of β -rays as is the case in the radium C and thorium C branches (*Phil. Mag.* 1914, (VI), 27,690; 28, 818). Confirmatory evidence appears to be desirable.

Note 12. *Actinium C''* is also called actinium D.

Disintegration of Radium.

Lead is viewed as the end product (Pitchblende invariably contains Lead), and with each change there is an outburst of energy (*cf.* also p. 332).

Ionium is an intermediate product between Uranium and Radium. Ionium present in commercial Uranium salts is identical chemically with Thorium and cannot be separated from it.—F. Soddy, P.J. i./12,394. *See also* the Thorium Disintegration Products.

RELATION BETWEEN THE URANIUM AND ACTINIUM SERIES.

Researches on the γ rays of Radium throw fresh light on the peculiarities seen in the absorption of these radiations and on their wave-length; and a beginning in the application of the Rutherford-Bohr model nuclear atom to the whole of the elements.—F. Soddy, Ann. Rep. Chem. Soc. 1919 (Vol. XV.), p. 195.

Ekatantalum (*Syn.* PROTOACTINIUM). *The Parent of Actinium.*

According to Prof. Soddy, "it was expected that Uranium-Y isotopic with Uranium-X, and Ionium in the Thorium place in the periodic table, and simultaneously formed with one of them in the dual α -ray change of either Uranium I. or Uranium II., would prove to be the first member of the Actinium series. Uranium-Y gives a β -radiation, and therefore its unknown product must occupy the Ekatantalum place in the periodic table and be isotopic with Uranium-X₂ or Brevium, the very short-lived product of Uranium-X, in a β -ray change."

There is no reason to doubt that Ekatantalum is the product of Uranium-Y, but this probably, as in the production of Uranium II. from Uranium-X₂, can never be the subject of direct proof owing to the unfavourable relations of the periods. There remains the doubt, however, as to whether Uranium-Y is the product of Uranium I. or Uranium II., although the latter is perhaps the more probable.

With exceptions the complicated disintegration sequences of the radioactive elements are now unravelled and are indicated in figures reproduced in the Ann. Rep. Chem. Soc., 1919 (Vol. XV.), p. 200.

The raw material for the preparation of Protoactinium is the insoluble residue, consisting chiefly of Silica, from Pitchblende after treatment of the mineral with Nitric Acid. It is recommended to add $\frac{1}{4}$ to 1% Tantalum Oxide to the residue and to heat with a little Concentrated Sulphuric Acid and excess of 40% Hydrofluoric Acid in a platinum vessel, properly cooled, then to dilute and filter through a paraffined funnel, evaporate the filtrate, and ignite gently. This renders the Tantalum Oxide containing the Protoactinium insoluble in acids. So far efforts to concentrate it from Tantalum have failed.—J.C.S.A. ii./20,147.

Isotopes are very closely related elements, chemically inseparable but with different atomic weights. At least six isotopes of lead are known which differ either in atomic or radioactive properties. A Table of Isotopes is provided in the Introductory portion of this Volume.

Neon is a mixture of isotopic elements of wts. 20 and 22. Chlorine is a mixture of at least two with wts. 35 and 37 and so on.—Aston, Na., Dec. 6, '19, and J. R. S., January 1920, p. 5.

The rate of change of radio-active elements is stated by Oswald in the words "*As time increases in arithmetical progression the quantity of substance decreases in geometrical progression.*"

Chemical Identity of Radio-Elements.

Uranium-X and radio-actinium are chemically identical with thorium; mesothorium-2 is chemically identical with actinium; radium-A is chemically identical with polonium; radium-C, thorium-C, actinium-C, and radium-E are chemically identical with bismuth; radium-B, thorium-B, and actinium-B are chemically identical with lead; thorium-D and actinium-D are chemically identical with thallium.—A. Fleck, Brit. Assocn., 1913.

Polonium.—This is another radio-active element discovered by Mme. Curie in Pitchblende, which gives off the α rays almost exclusively. Using a preparation of Polonium small enough it is possible to reduce the impacts of the α particles to 1 or 2 per second.

By aid of a loud-speaking telephone, it is said to be possible to hear Polonium breaking up into α particles (Helium)—the work of Mme. Curie.—P.J. i./24, 41.

Polonium is identical with Radium F. It has a half value of about 140 days. Polonium and Radium are present in a ratio of 1:5000.

The quantity of Polonium in a Radium mineral is 1 mgr. of Polonium for every 14 tons of Uranium.—For Mme. Curie's method of extraction, *see* Nature, Feb. 24, 1910, p. 509.

Since Polonium is the last of the active products in the radium series it is to be expected that it should be transformed into helium and lead, one atom of helium and one atom of lead from each atom of Polonium—this point of view is further substantiated by the fact that before the formation of Radium F. seven α particles are successively given off, each of which being an atom of helium has the atomic weight 4. Therefore the atomic weight of polonium would appear to be $(4 \times 7 =) 28$ less than that of uranium, i.e., $238.5 - 28 = 210.5$ —this loses an α particle, i.e., 4, giving a final atomic weight of 206.5—a value very close to that of lead.—Rutherford.

Radium rays are of (at least) three main types:—

(1) The α rays, non-penetrating and only slightly deviable in a strong magnetic field, deviation about $\frac{1}{10000}$ part of that of the β particle,—the direction being opposite to that of the β . (2) The β rays, moderately penetrating, deviable. (3) The γ rays, exceedingly penetrating, non-deviable.

When speaking of β and γ Radium rays what are really intended are the β and γ rays of Radium C and C₂. The emanation like Radium itself gives only α rays.—(*vide* table *antea*.) The whole of the β rays result in the later changes of the 'active deposit.'—Soddy.

The α rays.

These are demonstrated by Crookes' Spinharscope (*σπινθάρης*, a scintillation), and by Glew's Scintilloscope.

Ninety-nine per cent. of the total energy of Radium is due to the α rays, the β and γ being responsible for the remainder.

The α rays from Radium are complex—4 different types, each with a definite 'range' or distance it will travel in any absorbing medium. The most penetrating type according to Bragg travels in air at atmospheric pressure and ordinary temperature 71 mm. (just under 3 inches) and no more. This fact is made use of in a most convincing lecture experiment in which bare Radium Bromide is placed in the centre of a flask coated inside with Sidot's Blende (crystalline Zinc Sulphide), there is no marked effect until the air is rarified by means of a pump—at the first stroke of which the Blende begins to glow.—F. Soddy

The ranges of " α " rays in air vary from 70.6 m.m. for Radium C. to 27 m.m. for Uranium.—Na., July 20/11, 98.

The fastest α particle is completely absorbed by the time it has travelled two inches in air. As a general rule this particle travels further in light gases, e.g., Hydrogen, then in heavy, e.g., CO₂.—Rutherford, P.J. i./13, 767.

The α rays are absorbed by glass, mica, a thin sheet of aluminium, or indeed a sheet of note paper, or by three inches of air. Glass, however, can be blown so thin as to allow the radiation to pass. *Vide postea*.

The rays constitute electrically charged atoms travelling at 12,000 miles a second, each α particle being associated with 2 charges of + electricity. Crystalline Zinc Sulphide is very markedly sensitive to them though much less to the β . Barium Platino-Cyanide and

Willemite, on the contrary, are more affected by the β than the α rays. The mass of the α particle is about four times that of the Hydrogen atom and is enormous in comparison with that of the particles composing the β rays. The α particle is a Helium atom (*v. Helium*). This accounts for the feeble penetrative power of the former.

The 'law of density' governs the penetration of metals and other substances by these rays, the absorption being proportional to the density. Tin, however, is an exception both for the α and β rays; for the α it is about the same as aluminium, and for the β it is about three times as opaque as its density would indicate.

The question as to mass, or volume, of the preparation comes into consideration in the case of the α rays,—the more the surface is spread out the less absorption there is of α radiation by the substance itself. The α rays from 1 mgr. of Radium produce more electrical effect than the β and γ rays from 30 mgr., *e.g.*, in discharging a silk tassel.

Rutherford has shown that at the point where the α particle is no longer detectable it is still travelling at 5,000 miles a second. Beyond this fluorescent and electrical actions all cease simultaneously. It follows that α particles expelled at a velocity below 5,000 miles per second cannot be detected, doubtless there are such changes akin to radio-activity which may be proceeding without our knowledge.

All substances absorb α rays proportionally to the square root of their atomic weights, if elementary, or to the sum of the square roots of the weights of the constituent atoms, if a compound or mixture.—F. Soddy.

All α particles have the same mass and differ only in the initial velocity of expulsion whether expelled from Radium emanation, uranium, thorium, or any other bodies which expel them.

Rutherford succeeded in detecting Helium outside a sealed thin glass vessel containing Radium in vacuo—the glass being thin enough to allow the α particle to pass—this being a further point towards proof that the α particle is an atom of Helium. He has also counted the number of α particles expelled from a given quantity of Radium every second. A milligram emits 136 millions per second.—Soddy.

The α particle carries two atomic changes of positive electricity, *i.e.*, it is a divalent ion.

The speed of α particles is such that the life of each α particle is completed in about 1/1,000,000,000 second.—Sir W. H. Bragg.

A photographic plate contained in a special form of dark slide may be used in place of Willemite Screens to demonstrate positive rays, giving thus permanent records.—Sir J. J. Thomson.

The α particles expelled in any one type of disintegration travel with exactly the same velocity—which is gradually diminished to exactly the same extent for each particle in passage through a homogeneous absorbing medium, until the "critical velocity" 2.7% of that of light is reached. The ionisation produced in any given length of its path *increases* as the velocity of the particles diminishes down to the critical velocity, when all effects cease abruptly and the α particle is absorbed or passes beyond means of detection. The *range of the α particles* is, therefore, an important constant.—F. Soddy.

In **Luminous Paints** composed of Radium and Zinc Sulphide the Zinc Sulphide undergoes rapid deterioration—the rate of decay in luminosity is proportional to the amount of Radium present, but not exactly proportional. Radium paint made according to **Admiralty Specification** containing 0.4 mgr. of Radium Bromide or its equivalent (in 1 Gm. of Zinc Sulphide) has a luminosity of about 0.03 foot candles, while a paint containing half this amount of Radium has more than half the luminosity. The sample containing 0.4 will die at a much more rapid rate than the other—the weaker

preparation has a *much longer life*. This is not generally known. In the manufacture of radium paint the *a* particle is by far the most effective to use for bombarding Zinc Sulphide.

The *a* particle from Thorium 'D' has a longer range, 8.6 cm., than that of Radium (7 cm.)—the *a* particle will travel through this distance in air in not exceeding 1/1000th of a millionth of a second. The particle in question from Thorium 'D' is therefore more effective in producing luminosity, but against this is the disadvantage of the relatively short life as compared with Radium. If Mesothorium had a life equal to that of Radium, the half period of which is 2,000 years against 5.5 for Mesothorium, it would be advantageous to use it. **Old samples of Radium are better than others for making paints.—The explanation being that old Radium is richer in the disintegration product 'F'**—in fact the *a* radiation of Radium increases for the first 100 years. Ionium would be an ideal excitant—the radiation from this consists of *a* particles only and its half period is even longer than that of Radium.

The Presence of Mesothorium may be detected by a special form of **Glew's Scintilloscope**—the scintillations from Thorium occurring in *pairs* due to the fact that when Thorium emanation disintegrates it gives out an *a* particle by reason of which it becomes changed into Thorium 'A,' which in its turn in the fifth of a second gives out another *a* particle.

In making Radium paint the best method is to place a little of the mixed powder in a watch glass in a heap, moisten it with Turpentine and then add about an equal amount of Mastiche Varnish and apply with a sable brush, taking care that the crystals of Zinc Sulphide are not broken. **Spodumene**, a native form of lithium, exposed to radium rays is luminescent on warming. **Balmain's Paint** (Calcium Sulphide) is improved by the presence of traces of bismuth.—A. H. Glew.

For an account of Manufacture of Luminous paints, see P.J. ii./21, 185.

Chemical action of *a*-rays on Hydrogen Sulphide, Ammonia, Nitrous Oxide and CO₂. The last is only very slowly decomposed.—J.C.S.A. ii./20, 214.

The β Rays. β rays are deviable in an electric field. They consist of electro-negatively charged electrons (not atoms of matter like the *a* particles), infinitely smaller than the *a* atoms, and have a mass about $\frac{1}{1000}$ that of the hydrogen atom. This does not mean weight—it refers to inertia.

The β rays are 100 times more penetrating than the *a* rays, being reduced to half value by passage through 0.05 Cm. of aluminium. They are, however, *absorbed for the most part by 1 mm. of lead*.

3 or 4 m.m. of Aluminium or 1 inch of cardboard is sufficient to absorb all β rays, while γ rays have been shown to pass 20 Cm. of Lead or 2 feet of iron.—Rutherford.

The average velocity of the particles of the cathode rays in a Crookes' tube is 5,000 to 10,000 miles per second, that of the fastest of the β particles of Radium is as high as 170,000 miles per second, *i.e.*, approaching that of light, but in addition there are various types of "soft" feebly penetrating slowly travelling β rays—Soddy distinguishes these by brackets—(β) rays.

The *a* and β rays "ionise" the gas through which they pass, making it capable of conducting electricity. The Hon. R. J. Strutt devised a Radium Electroscope for showing the dissipation of the negatively charged rays. We described this apparatus fully in earlier Editions.

Silver (*q.v.*) emits a secondary radiation very similar to the radiation from Radium, *cf.* p. 295.

The γ Rays usually accompany the β rays, *i.e.*, analogous with the "X" rays which are produced by and accompany Cathode rays,

γ rays are identical with 'X' rays except as a rule far more penetrating. They are given off by Thorium and Uranium also, and are

about 100 times more penetrating than the β , being reduced to half value by 6 to 7 Cm. of glass or aluminium; they will pass through almost everything, even 7 centimetres of lead before being reduced to 1% of their original strength. According to Rutherford they can be detected after passing through 20 Cm. of lead.

They are about 10,000 times more penetrating than the α . When γ rays pass through matter, β radiation appears in its place, moving first in direction of the original γ but afterwards scattering in the ordinary manner of β rays. The penetration and therefore speed of the β radiation thus produced increases with the penetration of the γ radiation to which it is due.

Heat Evolution.—Half a grain of Radium Bromide evolves, according to F. Soddy, about 2 calories of heat every hour,—in 4 years 70,000 calories. Half a grain of coal gives out during complete combustion only about 250 calories so that in the period in question (4 years) Radium emits nearly 300 times the energy obtainable from the same weight of coal. 98% of the heating effect of Radium is due to the α particles.

It is unwise to keep radium in solution in a sealed vessel as the gradual production of hydrogen and oxygen may cause it to burst. Carbon Dioxide, Ammonia and Hydrochloric Acid are also decomposed by it.

Radium Emanation. Radon Rn.—222. *Syn. Niton (Ramsay) Nt.* = 222.4 (since altered to 222).

Radium gives off a gaseous emanation allied to the Argon family. It may be regarded as Radium that has lost an α particle. It should occupy one of the two vacant places in this group in the periodic table. It is inert,—not capable of absorption by chemical means. Niton disintegrates in definite stages, and in doing so gives out the various rays—see Table *antea*. It is void of chemical activity, and follows Boyle's law. Its boiling point at standard pressure was found by Rutherford to be -65°C . Gray and Ramsay considered the emanation cannot exist as a liquid below -71°C .

The gas is given off without appreciable loss of weight of the original matter, and can be aspirated through a tube and be made to condense at -150°C by freezing with liquid air.

Itself strongly luminous, it causes Willemite to glow brilliantly in the dark. It can be filtered through wool as distinct from cathode particles, *v. p.* 291. It was found by Sir W. Ramsay and Prof. Soddy to give the helium spectrum on keeping three or four days; in fact, the emanation changes into helium.

Ramsay found that in 3.7 days the amount of luminous gas was only half its original size, and in thirty days it was only the smallest pin-point in the tube.

This reduction in volume is concurrent with the change from the gaseous to the solid state (*v. Table ante*). When a Radium Salt is dissolved in water and the liquid evaporated to dryness, the Radium will be found to have lost the greater part of its radio-activity, *i.e.*, the intensely radio-active Emanation will have passed off on dissolving in the form of a gas, unless steps are taken to prevent its disappearance. The β and γ rays will have disappeared, and the α rays would be only a quarter as powerful as initially—the activity, however, gradually recovers in a month. The energy of the Emanation is three times as great as the Radium from which it is obtained.—F. Soddy.

The Emanation decomposes water, hydrogen being 3% in excess and will cause the gases to recombine.

The volume of Helium produced from 100 volumes of emanation is about $3\frac{1}{2}$ volumes, agreeing with the view that the α particle is a Helium atom.—Ramsay.

An atom of Helium and an atom of Emanation are simultaneously expelled when an atom of Radium is disintegrated, but when the quantity of Emanation has reached its maximum it does not accumulate further with further lapse of time. The Emanation is absorbed by cocoanut charcoal (*q.v.*) at ordinary temperature and pressure. On heating the charcoal the emanation is driven off, and can thus be concentrated. This has been used for extracting the Emanation always present in the atmosphere.

Standards for Radium Emanation.

The unit of Emanation is called the 'Curie' and is the quantity of emanation in equilibrium with 1 Gm. of Radium (element) with the sub-divisions 'Millicurie' and 'Microcurie'—the millicurie being equivalent to 1 mgr. and the microcurie to 1/1000 mgr. on these lines.

Other more or less arbitrary standards not now officially recognised are the **Gram-second** and **Milligram-minute**. The former is the amount of emanation freed from 1 Gm. of Radium element during 1 second.

The **Mache Unit** used for measuring the small amount of electricity in certain radio-active waters depends on the saturation current leak through an electro-scope due to the emanation and its products Radium A and Radium C. *It is the quantity of radio activity which causes a leak of 1/1000 of an electrostatic unit of current intensity.*

The Mache Unit is a minute one whereas the Curie is a large one. The emanation combined in 10 litres of Mineral Water moderately radio-active is of the order 0.1 Microcurie.

The Units compare as follows:—

Curie;	Millicurie.	Microcurie;	Milligram-minute,	Mache.
1	1,000	1,000,000	7,992,000	2,500,000,000
0.000001	0.001	1	7.992	2,500

1 'Electrostatic Unit' = 1,000 Maché Units. cf. B.M.J. i./13,118 & ii./13,1107.

A slide rule for Radon dosage calculations.—W. V. Mayneford, B.J.R., Dec., '28.

Induced or Excited Radio-activity.

Solid substances in the immediate neighbourhood of a Radium Salt acquire **Induced Activity**. After removal the activity decays abnormally rapidly at first, but subsequently in geometrical progression: $\frac{1}{2}$ value 30 minutes. Induced Activity consists of α , β and γ rays. It is in the form of an "Active deposit." In this active deposit changes take place several times in quick succession. The bodies are termed Radium A, Radium B, Radium C, Radium C₁, and Radium D.

In the case of **Thorium** the induced activity lasts a few days, whilst that of Actinium decays slightly more slowly than that from Radium.

Secondary β radiation may be well shown (Glew) by placing a tube of radium above a photographic plate face downwards on a piece of metal, *e.g.* Platinum covered by a piece of black paper; there results darkening of the plate. The photographic efficiency of this secondary radiation is greater than that of the primary radiation which has already passed once through the film.

The hardness or penetrability of secondary rays produced by impact of Radium rays is governed by the Atomic Weight of metal giving rise to them.—F. H. Glew, J.R.S., Oct., 1912.

Substances such as Lead Foil or common Salt placed in the neighbourhood of Radium become coated and can be similarly used for superficial applications. Sodium Chloride so treated is sometimes dissolved in water and used for injection purposes.—W. E. Dixon, B.M.J. i./29,239.

Helium (He=4) is occluded in various minerals especially those of Uranium and Thorium. This suggested to Ramsay and Soddy the investigation which led to the proof that radium emanation is in part helium.

In some instances its volume is nearly 100 times as great as the volume of the mineral from which it was obtained.

Helium has been liquefied at—270° C., *i.e.*, only 3° from the absolute zero.

Helium is one of the ultimate products developed by nature from Radium, Uranium and Thorium, formed slowly but, nevertheless, fast enough to ensure that all minerals containing these elements must contain Helium also. The α particle from Radium is an atom of Helium. There is simultaneously an atom of Radon produced (*vide a Rays antea*).

Taking the atomic weight of Helium as 4 this inert gas fits in with other members of a like nature, *viz.*, Neon At. Wt. 20, Argon 40, Krypton 83, Xenon 130.

50 mgr. Radium, it has been stated, produce 0.000018 mgr. Helium in 60 days, or 0.0022 mgr. in 1 year from 1 Gm. of Radium Bromide. About 2 mgr. of Helium are produced from 1,000 tons of Uranium per annum. It is possible

to draw conclusions as to age of geological formations from the accumulation of Helium in them.

F. Soddy detected the production of Helium from Uranium and Thorium—the amount is 1,500,000,000,000 of the Uranium or Thorium per annum which accords with theory. The method of detection depends on the use of strongly heated Metal Calcium, which *in vacuo* absorbs all gases except Helium.

An analysis of the atmosphere shows that one cubic metre contains

Argon	9.323	litres
Neon..	18.1	c.c
Helium	5.4	c.c.
Krypton	0.049	c.c.
Xenon	0.0059	c.c.

Professor Moureu has definitely established that the rare gases are present in the external atmosphere surrounding the earth, and also in the air found in the interior of the earth. C.D., Jan. '23, 869.

Commercial Use of Helium.

Helium is present in gases, minerals, springs—at some springs in France as much as 5% is present. Prior to 1918 the total amount isolated did not exceed three or four cubic metres. It is twice as heavy as Hydrogen (the atmosphere being 14.4). **Next to hydrogen it is the lightest gas known.** It enters into no combinations, and is quite inert; it is non-explosive. It was suggested in 1914 to fill envelopes in air ships instead of Hydrogen. Its rate of diffusion through the envelope is 30% less than that of Hydrogen. At Bow Island a supply of 10,500,000 cubic feet is available annually. It is conveyed by pipes to Calgary where first Nitrogen with a content of 5% Helium is obtained, while liquid Methane, Pentane and Butane are also produced in large amount. By submitting this 5% Helium to a temperature of —163 at a pressure of 25 to 30 atmospheres Helium of 87 to 90% purity is isolated, and this can be further purified by means of liquid air. Hydrogen with a content of 20% Helium is still non-inflammable.—Prof. J. C. McLennan, J.C.S., July, 1920, 923; C.D. '20, 845; L. i./20, 164; Na. May, 20/20, p. 360; Aug. 12/20, p. 747.

30,000 to 40,000 cubic feet are extracted daily from natural gas in the U.S.A. It is compressed in steel cylinders and stored, and its export is prohibited. Sir E. Rutherford succeeded in converting a certain amount of Nitrogen into Hydrogen by bombarding the gas with the nuclei of Helium atoms in the form of α -Rays. It possesses 92% of the lifting power of Hydrogen. Mercury at the temperature of liquid Helium (490° F. below the freezing point of water) has a remarkable super-conductivity. No natural gas within the Empire has been found to contain as much as $\frac{1}{2}$ % of Helium, whereas in Texas gases containing 1 to 2% are available.—Prof. J. C. McLennan, J.R.S., Oct., '24, 171.

Transmutation of Hydrogen.

Norman Collie & Patterson independently found indication of **production of Neon & Helium from Hydrogen** on subjecting the latter to bombardment by Cathode rays. This, if correct, would be a case of *synthesis* in contradistinction to breakdown as in the disintegration of Radio-active bodies.

Sir William Ramsay found that on treating water with Radium Emanation he obtained Neon in addition to Helium. The equation $\text{He (4)} + \text{O (16)} = \text{Ne (20)}$ may be the explanation.

In Bath waters there is three times as much Neon as Helium, Niton decomposing in the bowels of the earth and the nascent Helium uniting with the nascent Oxygen to form Neon. Ramsay also showed the production of Argon when Sulphur and Hydrogen are subjected to Cathode Rays for 4 or 5 hours and of Krypton when Selenium and Hydrogen are treated in the same manner. He viewed the change of Hydrogen to Helium as polymerism. It is possible that Xenon may be formed by action of Cathode Rays on Tellurium in presence of Hydrogen.

Copper Salts under influence of radio-energy yield, it is said, distinct traces of Lithium.

In response to criticism, Professor Collie stated he was satisfied that Neon and Helium have been produced from substances in which they were previously not present. In the case of Radium the degradation cannot be hastened or checked, but this artificial production of Helium and Neon is at the other end of the system—at the bottom of the list of low and of the lowest Atomic Weights.

Prof. F. Soddy says he traced the Helium in vacuum tubes to the Aluminium electrodes.

Hon. R. J. Strutt has been unable to confirm the work of Collie and Patterson. This may be due to the difficult conditions of the work.

The duration of geological time suggested by the study of radio-active minerals is of the order of 500 million years.—*Na.*, July, 1911, p. 9.

Radio-activity may be regarded as one phase of the cycle of evolution of matter—the other phase—the construction is infinitely slower. The radio-active phase is virtually the culmination of the long constructive phase during which atomic complexity has increased to such an extent that it eventually leads to instability.—*B.M.J.* ii./11, 1546.

Atomic energy.—If Hydrogen could be transmuted into Helium energy could be produced in quantities prodigious beyond the dreams of scientific fiction. For 1 gram. atom of Hydrogen, *i.e.*, the amount contained in 9 Cc. water, the energy expressed in terms of heat is 1.6×10^{11} calories, or in terms of hours 200,000 kilowatt hours. There is enough power in a tumbler of water to drive the "Mauretania" across the Atlantic and back at full speed.—*F. W.* Aston, *B.J.R.*, Jan., '26, 12.

Radium in the Atmosphere is present to the extent of 60×10^{-12} Gm. per cubic metre. The air in the upper atmosphere (10 to 50 miles up) has been shown to be considerably ionised, possibly due to the direct radiation from the sun which consists of α β and γ radiations *inter alia*.—Rutherford

Action on Bacteria, Toxins, Ferments, Blood, etc.

The fact seems to be clear that Radium Rays are not bactericidal to any extent. L. Barlow, however, detected a bactericidal action and predicted the use of Radium in bacterial diseases in addition to malignant growths.

In a series of experiments upon diphtherial Toxins quantities of Radium Sulphate varying from 20–50 micrograms and the duration of contact with the Toxin being thirty days—with non-radiferous Toxins the "control" guinea-pigs died within from 24–72 hours after inoculation, but the animals inoculated with the radiferous substance survived at least for 5–12 days, and in some cases for 20–30 days. A similar difference between the action of the radiferous and non-radiferous Toxin was discovered with emulsions of the living Koch Bacillus. Radium has no retarding influence, however, on the virulence of Tetanic Toxin.—*B.M.J.* ii./11, 1025.

Radium is stated rapidly to destroy the ferments emulsin, pepsin, trypsin, and ptyalin.

Blood *in vitro* mixed with Radium emanation. Hæmolysis occurs with gradual conversion of oxyhæmoglobin into met-hæmoglobin. The hæmolysis is due to α -radiation. Leucocytes show marked degenerative changes when exposed to α -rays. The specific properties of opsonin and hæmolytic complement are lost when serum is exposed to α -rays. The progressive changes caused by these rays indicate the separate identity of opsonin and complement. The β and γ rays yielded negative results in analogous experiments.—H. Chambers and S. Russ. *Roy. Soc.*, June, 1911, *per Na.*, June 15, 1911, p. 540.

Radio-active bodies are probably poisonous, acting directly on the nerve centres. If radium emanation were used criminally the excited activity would have to be sought for, and probably would not be found, whereas if an actual radium salt had been administered even the ashes of the dead body would show the necessary radio-activity to convict the murderer.

α , β and γ rays of Radium arrest acetous fermentation in dose of 1 microgramme per cent. of liquid; a smaller dose accelerates fermentation.—Laborde, *Jl. Pharm. Chim.*, 1922, 26, 44; *Y.B.P.*, '23, 147.

THERAPEUTIC USE OF RADIUM.

Distance of the Part to be irradiated, from the Radium.

As with light, "X" rays and other forms of Ether vibration, the strength of the radiations *varies inversely as the square of the distance*, *e.g.*, if an object be 1 Cm. from the Radium and another 5 Cm. from it, the latter will only receive 1/25 the strength of radiation of the former. If the Radium be 5 Cm. from the skin, this and the tissues

5 Cm. below the skin should receive exactly $\frac{1}{4}$ of the radiation received by the surface, but the intensity is greatly diminished owing to absorption. See also *R. Knox* under *Screens*.

Columbia Wax (see also p. 343), is used for supporting tubes. A preparation of this kind is Beeswax 100, Hard Paraffin (M.Pt. 62° C.) 100, Fine Saw Dust 20.

Histological changes effected by radiation—initially on normal skin there is stimulation—the nuclei showing enlargement and alteration in shape, the stroma swelling—the more superficial cells may die, the epidermis meanwhile peeling off. The cells lining sebaceous and sweat glands and hair follicles undergo granular degeneration and die too. In the deeper layers normal cells are first replaced by others of embryonic type and these evolve into ordinary connective-tissue cells. Finally, at the end of some months, the general structure is that of fibro-elastic tissue. In the case of new growths the changes effected are similar, with exception that the neoplastic cells instead of being stimulated have their vitality lessened; their evolution ceases and clumps of cells undergo necrobiosis—meanwhile normal structures in and around the growth show increased vitality. With regard to the neoplastic cells their decrease is probably due to alterations in the blood supply. In any case if treatment has been successful the site of the original growth becomes occupied by layers of fibrous tissue, or in the case of a more or less circumscribed tumour, by a body resembling an innocent fibroma.—*Barcat and Dominici*.

Muscle-nerve preparations of the frog, effects on. Under α rays the irritability of the muscle-nerve preparation was apparently longer preserved than under control conditions, β and γ rays were without effect. No histological changes found.—*Lazarus Barlow*, L. ii./12, 1508.

Distribution and Excretion of Radium and its emanation after administration.

Experiments on mice showed:—

After the administration by mouth or by injection of radium a widespread radio-activity throughout the body. Elimination of Radium principally by the bowel and in a minor and slower degree by the kidneys. Its constant presence in the lungs after inoculation suggests that an accumulation of Radium takes place with a view to the more ready excretion of the emanation. After administration of the emanation, and however introduced, a general radio-activity of brief duration is caused throughout the body. Elimination of the emanation takes place principally by the lungs, and to a very slight extent by the kidneys. Soluble salts of radium are rapidly eliminated, however given. The insoluble salts *per os* are excreted directly by the bowel and there is no evidence of temporary absorption. When given by injection, slow elimination takes place by the bowel, but the time taken is so great that the salt may be considered to be permanently present at the site of injection. The elimination of the emanation occurs rapidly, and was complete, after powerful doses, in four hours.—*E. Bellingham Smith*.—*Qr. Jl. Med.*, Jan., 1912, p. 249.

Chemical Effects produced by Radiations.

It is undesirable to introduce unprotected Radium Salts (or Thorium Salts) into the system. Apart from poisonous action at any rate of the latter, these may remain permanently in the system and destroy surrounding tissues.—*Rutherford*.

Radium Emanation being a gas, and directly concerned in the production of the greater part of the activity of Radium, it is essential that Radium Salts after preparation in their final form, should be kept in hermetically sealed tubes from the air, as otherwise, by the escape of Emanation, much of the activity of the preparation is lost.

In the early work rodent ulcers of superficial origin, lupus, epithelioma and papilloma were cured by juxtaposition, *e.g.*, by placing one or more 5 milligram glass tubes in contact with the part for various successive lengths of time.

Simple conditions, *i.e.*, chronic inflammatory lesions, ulcers, *nævi*, can be treated with accuracy, while conditions verging on the malignant, *i.e.*, the rodent ulcer and epithelioma are more intractable.

The *Wave Length* is the *fundamental principle* of radiation therapeutics. When the correct wave-length for a particular depth has been estimated, it is then merely a matter of time—*i.e.*, duration of exposure—to produce a particular effect on the tissues. The effect is dependent on the power of absorption possessed by the tissue. With regard to the relative values of X rays and Radium rays, we must assume that we are dealing with radiations having a very wide range of wave-length, the γ ray of Radium representing the extreme limit of penetrating power. Given an equal wave-length from either agent, the effect will be the same. The X ray value is limited by the inability to produce X rays equal to the γ radiation of Radium. The voltage required to produce X rays equal to the hardest γ rays is between 1 and 2 million.

WAVE LENGTHS.

The following estimations have been made :

Hard γ rays..	..	Between 0.01 and 0.001	Angström	Units.
X rays	Between 0.10 and 0.05	„	„
Visible light..	..	7,200 to 4,000	„	„
Ultra-violet light	4,000 to 200	„	„
Longer radiant heat waves beyond the red..	..	0.06 m.m. to 7,600	„	„
Hertzian or Wireless waves	Follow on.		

—From a paper on Radium Therapy, R. Knox, B.M.J. i./22,631.

1 Angström Unit = 10^{-8} c.m. This is equivalent to one ten millionth part of a millimetre.

NON-MALIGNANT CASES. Greatest care to be taken in treating so called port wine stains. Radium suggested for angiomas. Uterine fibroids and hæmorrhage. Subacute and chronic leucorrhœa. Inoperable hypertrophic goitre. Exophthalmic goitre. Leukæmias. Cataract and tuberculous adenitis.—R. Knox, B.M.J. i./22,631.

MALIGNANT DISEASE.—In *skin cancer*, Radium the agent of choice when operation is decided against. *Epithelioma*, being difficult to control, yields only palliative results. Cancer of the *lip*, when springing from the skin surface, is occasionally treated. Of the *lingual* and *buccal* mucous membrane is treated with Radium and fulguration. No sharp cutting instrument should be used in this region. Malignant diseases of the *antrum* should be treated, operatively *plus* Radium. Of the *oesophagus*, if in very early stage, of the *stomach* and *intestinal tract*, surgery followed if possible by radiation. Early cancer of the *breast*—Radium has rendered seemingly impossible cases operable. Of the *rectum*—not well treated. Of the *prostate*—should be removed, if early, and Radium tubes and needles buried at the time. Of the *fundus uteri*—a surgical condition, if the patient is able to stand operation, otherwise a case for Radium.—R. Knox, B.M.J. i./22,631; see also R. Hughes Parry, Arch. Radiol., '24,29,3.

Radium for Cancer, Med. Res. Council, Ann. Rept., 1927-8.

During the last seven years random empiricism has been replaced by definite technical methods for the treatment of cancer by Radium in almost every region of the body except the stomach. There is now a widening circle of real interest in Radium therapy among

surgeons. **Early cancer of the neck of the womb can now be removed** locally by Radium **as surely as by the knife** and with less risk and suffering. Radium is now proved the best means of treating 'inoperable' cancer of the mouth or tongue, and in 'operable' cases it will soon replace excision. Confidence in Radium treatment is rapidly gaining ground in respect of cancer of the breast in women and of the rectum in men. The progress is only the beginning of an accelerating advance, but there is at present a wholly inadequate supply of Radium in the country and a shortage of trained operators and available beds.—L. i./29,629. *See further data under Metal Tube and Screen Results—postea.*

Irradiation of living cells shows effects in three stages. (1) increase of cell activity, accompanied by, it may be, proliferation (2) arrest of cell activity (3) degeneration and destruction of the cell. These merge one into the other and the Therapy depends on their properties.—B.M.J. ii./23,28; L.i./24,344

Pioneer Work :—

The late Sir J. Mackenzie Davidson reported many cases of rodent ulcer treated without a failure.

Dawson Turner reported on 41 cases treated by Radium during 1912 at the Royal Infirmary, Edinburgh. Tubes inserted into growths wherever possible and left *in situ* for up to 12 days with simultaneous external use. Of 11 nævi two were port wine stains, seven cured, three under treatment and one (port wine stain) did not return. Rodent ulcer extraordinarily amenable. Radium is superior to Carbonic Snow or Zinc ionisation or excision, because the rays penetrate deeply. Secondly, the treatment is painless; thirdly, cosmetic results good.—B.M.J. i./13,606; L.i./13,817; L.i./17,546.

It was soon found in the early pioneer work that the only rays that can be usefully employed for malignant growths are the hard β and γ rays—the α and soft β are to be filtered off.

Epithelioma of the tongue and lip, nævus, port wine stain, pigmented mole, hairy mole, angioma of the eyelids, keloid, are stated to have been cured.

OCULAR THERAPEUTICS.—Sir Arnold Lawson and the late Sir J. Mackenzie Davidson reported 46 cases. **Method of Application.**—Sealed glass tubes (permitting only β and γ rays to pass) applied direct to affected part—the tubes to be kept in close contact. The eye is first cocaineised.

Length of exposure.—5 minutes was fixed as being absolutely safe. A tube of 20 to 30 mgr. can be applied to the inner surface of the lid in rodent ulcer affecting the lid border and so lie in contact for $\frac{1}{2}$ hour. No ill effects nor aggravation of symptoms. Pain usually transient. Lesions of the cornea can be treated successfully with five minute dose by the same amount, which for affections of skin and lids required an exposure three or four times as long. Superficial lesions of the cornea can be treated by five or ten mgr. applied once or twice. 20 mgr. is sufficient to combat any external affection of the eye and eyelids in which Radium is likely to be of service. The scars produced—e.g. in cases of spring catarrh—are supple and smooth without the slightest tendency to cause cicatricial dragging, but they are very blanched.

The following approximate sub-division (initiated in earlier editions) into 'Tube or Needle' and 'Spread Surface' results, is retained. The data should be compared, however, with the latest information on Radium Containers (Tubes, Needles, Plaques, etc)., postea.

(1) Metal Tube or Needle (inserted into Tumours) and Metal Screen Results.

Deep seated or deeply extending growths can be cured by Radium radiations from which the less penetrating rays are filtered out. Large recurrent scirrhus of breast and epithelioma of larynx treated with success. 56 mgr. of pure Radium Bromide in silver tube 0.6 m.m. thick advised, placed in two different positions during the treatment.

Action at a depth is obtained by using large quantities of Radium and filtering out all the less penetrating radiations and giving long exposures. The question of success with Radium treatment appears to depend on structure and clinical characters.—Finzi.

The following are in approx. alphabetical arrangement.

CARCINOMA OF CERVIX.—Heavy metal screens not necessary. In no case need a screen thicker than 1 mm. of Silver be employed unless huge doses are given. Method of use at Manchester.—A. Burrows, B.M.J. ii./21,522. See also *ibid.* ii./22,33.

Not justifiable to advocate the treatment in uterine cancer in lieu of surgery in operable cases, though often of great use in borderline cases. In inoperable cases, Radium produces a degree of symptomatic improvement. Progress of the disease checked.—A. E. Hayward Pinch, B.M.J. i./21,881.

Results in uterine cancer do not yet equal those of surgery.—Douglas Drew, B.M.J. ii./21,58. Can be relieved of hæmorrhage, discharge and pain.—S. Forsdike, B.M.J. ii./21,129.

Cancer of cervix—50 cases treated with Radium at St. Bart's Hospital. Hæmorrhage and vaginal discharge ceased. Life prolonged in inoperable cases. 173·6 mgr. of element employed in some cases. 24-hour results better than 8-hour. Disappearance of growth from the cervix within a few weeks.—M. Donaldson and R. G. Canti, B.M.J. ii./23,12.

Inoperable carcinoma of cervix treated.—M. Donaldson, B.M.J. i./25,876. See also G. I. Strachan, *ibid.* 879. At Cancer Hospital, London.—P. H. Cole, B.M.J. ii./25,831; see also M. Donaldson (Bart's), *ibid.* 836; S. Forsdike (Soho Hospital for Women), *ibid.* 839.

There is less primary mortality, less morbidity, less loss of time, with Radium therapy than in radical operation. Palliative results in cases not permanently cured an advantage. Vesical and rectal FISTULÆ should be less frequent in Radium therapy as technique develops. Repeated irradiation of distinct value. A monthly follow-up is essential. Large amounts of Radium not necessary to produce results.—G. G. Ward, B.M.J. ii./28,609.

In five years' time the knife will be of secondary importance in cancer. Radium has established its superiority over X-rays and is entering on a struggle for supremacy with the knife. The growing part of a tumour is its edge, the interior being composed of old degenerating cells; the first must be attacked. In TONGUE cancer the number of three to five-year cures already equals, or surpasses, that of cures by the knife: in carcinoma of the RECTUM the knife is only an adjunct to Radium: in breast carcinoma Radium is supreme in secondary growth which can be completely dispersed by it, and it checks the advance of inoperable cancer—do away with the vision of the knife, and patients will come earlier in the disease.—D. C. L. Fitzwilliams Pr., Nov., '28,286-290.

A sad disproportion between the needs and the supplies in all quarters of the country. In the treatment of primary cancer of certain sites, *e.g.*, the tongue and cervix, Radium has largely **taken the place of surgery**, and the results obtained in some areas suggest that it is now no longer necessary to regard 'inoperability' as always synonymous with 'incurability'. The need for knowledge of the proper administration of Radium is as pressing as the need for Radium itself: instructions should be introduced to the curriculum of all teaching centres, and hospitals or clinics should be established for full-time study of Radium treatment. To continue to be content with the present grossly inadequate supplies in this country is to play with an issue of national moment—it is beyond the scope of private donation and subscription, the problem is a national one.—A. B. Smith and S.M. Smith Pr., Nov., '28,307.

In 41 cases of uterine fibroids the insertion of screened Radium into the uterus resulted in cures in 88·2%, improvement in 5·8%, and failure in 5·8%. Of 209 cases of uterine bleeding so treated on the basis of follow-up reports 50% of which were made after 5 years or longer, 93·3% were cured.—J. R. Linton and Co-workers, Jl. A.M.A. i./29,968.

'Bomb' treatment likely to prove the method of choice in Radium therapy, but high cost and restricted supply of Radium require urgent attention. Economy necessary—work should be specialised in special institutions, and 'night' and 'day' staffs employed.—A. H. Burgess, Pres Address, B.M.A., '29, B.M.J. ii./29,134.

Radium Teletherapy—clinical experience with a temporary 'bomb.'—E. R. Carling and A. J. Leslie-Spinks, B.M.J. ii./29,180.

Radium Treatment of Cancer in France and Belgium.

In contrast to the tendency in English practice, little attention is being paid to Radium emanation: the chief line of progress is in the use of gamma rays from a distance by aid of adherent wax support (Columbia Wax). In the case of malignant disease of glands of the neck, for instance, a collar of wax from 1 to 3 cm. thick is moulded to the neck and shoulders and Radium needles in Platinum are embedded in the outer surface of the wax: the face is protected by a lead screen embedded in the wax cast. The beta rays are absorbed by the wax and the patient receives pure gamma radiation. In Brussels a thin case is used for the purposes, moulded to the contours of the body, and made of shavings of lime-wood glued together, the tubes of Radium being supported at a distance of 5 cm. from the body surface, and equidistant from one another, by blocks of cork or light wood attached to the case. The standardised treatment of cancer of the cervix, which gave excellent results, consisted in the insertion of a Lead tube, containing a large dose of Radium, into the cervical canal, smaller amounts being packed into the lateral fornices: these were left five or six days and then heavy doses of deep X-rays given as a routine.

There are 15 regional cancer centres distributed throughout France, directly under the control of the Ministry of Health, a large supply of Radium being concentrated at each centre, and a total of 31½ Gm. being available. France has 'seized Radium with both hands, and is far ahead of us in organisation.'—D. J. Armour and H. S. Souttar, L. i./29,299. The use of Columbia Wax is well known in this country, and the Brussels 'shavings' method is being substituted in London by the use of plastic wood.—E. R. Carling and Stanford Cade, L. i./29,363.

The following conclusions were arrived at from a study of 418 cases. (1) Patients with carcinoma free from necrosis and of limited extent, may be safely given the total radiation dose within the shortest practicable time. (2) Patients with extensive and necrosing carcinoma should be treated with fractional doses at definite intervals. (3) Patients with extensive carcinoma almost filling the small pelvis, or with large necrosing areas and advanced cachexia, should not be subjected to a full course of Radium treatment. Bleeding arrested by small dose of filtered Radium. (4) Recurrences, following the application of a correctly-measured and full Radium dose, should not receive further Radium treatment.—H. Schmitz, per B.M.J.E. ii./24,67.

Combining operation with Radium treatment of cancer. It is an advantage to bury Radium tubes and needles in the incised area and paths of dissemination.—W. C. Stevenson, L. ii./26,1158.

CANCER OF BUCCAL CAVITY TREATED.—Stanford Cade, L. i./29,8.

CARCINOMA OF LARYNX.—A large window is made in the thyroid cartilage and 5 to 10 needles inserted, lying parallel and vertical. The needles are 1 to 2 cm. long, containing 0.5 or 1 mgr. Radium element, a 0.5 mm. filter of Platinum being used with a small percentage of Iridium. The needles are left *in situ* for 6 or 7 days. In early cases, where the disease is strictly localised to a vocal cord, a high percentage of cures can be expected and after results are far superior to those obtained by operation. In advanced cases Radium should always be tried before laryngectomy.—N. S. Finzi and D. Harmer, B.M.J. ii./28,887.

CARCINOMA OF RECTUM treated by gamma radiation.—C. P. G. Wakeley and H. A. Colwell, L. i./29,553; see also Sir C. Gordon-Watson, B.M.J. i./29,671.

Small amounts of Radium for prolonged periods are more likely to be beneficial than large amounts for short periods. In treating a LYMPHOSARCOMA—perhaps the most susceptible of all growths to Radium—of the size of an orange, it would be best to have 100 mgr. Radium in 5 or 10 mgr. portions in separate tubes, to be distributed throughout the mass.—Dawson Turner, B.M.J. i./23,100.

CATARRHAL OTITIS MEDIA.— β and γ Radium rays or emanation, if properly filtered, have the power of softening, and rendering pliable, dense sclerotic tissue.—Sir Wm. Milligan, Pr., Jan., 1921.

DENTAL ASPECTS of Radium Therapy.—B.M.J. i./29,646.

FISTULA, ANAL cured.—A. Hallium, per Clin. Jl., May 30/23,204.

GRAVES' DISEASE and **HYPERTHYROIDISM** successfully treated with relatively small doses of Gamma Rays (Radium and Mesothorium). One or two exposures usually sufficient. No severe reaction and patient may return to his occupation at once. Especially suitable in non-operable cases.—B.M.J. *i.*/25,12.

LUPUS-EPITHELIOMA treated. Radium tubes screened with 1 mm. with rubber protective, the latter being later discarded. 284 mgr. applied for 11 hours.—F. Joselyn Jauch, *L. ii.*/21,704.

LUPUS in the nose successfully treated.—H. Baumgartner, per *Clin. J.* Nov. 28/23,574.

An exposure of at least 100 hours with a full-strength unscreened apparatus is necessary to kill T.B., but such exposure is impossible for the tissues. Cultures which have a fairly short radiation have their vitality inhibited. It is probable that the radiation of a lupus patch for a moderate length of time weakens the vitality of the tubercle bacilli and so enables their ingestion by phagocytes.—H. M. Wharry and O. Teichman, *L. ii.*/25,1277.

MENORRHAGIA.—Intra-uterine application of Radium should be employed for all cases, whether associated with menopause or with the presence of small fibromyomata in the uterus, or in young women with no signs of general or pelvic disease.—*Arch. Radiol.*, '23,47.

Menorrhagia treated. Screened with 2 mm. of Lead and 3 mm. of Rubber for emanation tubes, and 1 mm. of Platinum and 2 mm. of Rubber for tubes containing the element. Dosage of emanation 2,000 to 2,400 millicurie hours. Dose 2,000—2,400 mgr. hours.—G. Blacker, *L. i.*/23,421.

METORRHAGIA successfully treated.—*Clin. J.*, May 16/23,237.

NON-MALIGNANT UTERINE BLEEDING. Disagreeable sequelæ resulting from intra-uterine radiation.—F. J. McCann, *Pr.*, Jan., 1921.

Radium treatment safer, almost as certain, and preferable to hysterectomy. The ideal treatment in extremely nervous and elderly patients. Radium might be of use in producing artificial menopause in patients with pathological blood disease, with a view to conserving their blood supply.—E. F. Murray *B.M.J. ii.*/28,610.

For severe, persistent **UTERINE HÆMORRHAGE**, Radium preferable to either X-rays or hysterectomy,—inflammatory disease of the tubes and ovaries the only contra-indication. The Radium was placed in the uterine cavity and only the γ -ray utilised, the amount used varying from 50 to 100 mgr. In 3 cases, 50 mgr. used for 5 hours; in the others, 100 mgr. for 24 hours.—S. Forsdike, *L. i.*/23,1309. See also G. H. Varley, *B.M.J. i.*/24,317; also D. W. Roy *ibid.* 496.

Uterine flooding well treated by Radium Barium Chloride in Silver tube 0.6 mm. thick, pushed into the uterine cavity. In a young woman, a dose of less than 800 mg.h. should be given, but in a menopausal case as much as 990 mg.h. may be given and treatment repeated in 6 weeks. Contra-indicated (1) where fertility is important, (2) when myomata are present, (3) where there is chronic inflammation of the appendages.—B.M.J.E. *ii.*/24,84.

Dangers of intra-uterine application.—Per *Pr.*, May, '26,387.

MIDDLE-EAR DEAFNESS.—Selected cases substantially improved with 2 to 4 applications of 50 to 60 millicurie hours. Only one ear irradiated.—W. Hill *B.M.A. Ann. Meeting*, *B.M.J. ii.*/28,309.

MIKULICZ'S DISEASE.—A peculiar symmetrical disease of the lachrymal and salivary glands. The glands are converted into tumours thrusting them out of their normal position and deforming the face. Cross-fire treatment with Radium effectual in two cases agreeing with the data known on the disease. Half-strength applicators containing in all in one case 120 and in the other 240 mg. of Radium, the total exposures being respectively 25 and 30 hours.—A. E. Hayward Pinch, *B.M.J. ii.*/26,586.

MYELOID LEUKÆMIA.—Large doses of Radium applied to the spleen have given good results in the treatment.—Per *Pr.*, *Apl.*, '26,332.

PROSTATIC HYPERTROPHY.—In cases unsuitable for operation the condition may be improved, the Radium introduced in a urethral catheter containing two canals, a lower one for the Radium tube and an upper one to allow urine to escape. Treatment causes marked shrinkage of the enlarged gland. Two or more applications are generally necessary.—B.M.J.E. *i.*/25,81.

TUBERCULOUS ADENITIS treated by Radium. Response very satisfactory.—P. Gosse, *L. i.*/26,862.

A number of older abstracts are now removed. See 17th and 18th Edns

(II.) 'Spread Surface' (Plaque) Results (*Mainly*).

By spreading a minute quantity of Radium over a large area, the thin film gives α rays essentially free from β and γ , since the two last from a small quantity are practically negligible.—F. Soddy.

In spite of this clear statement of the fact 'spread surface' irradiation has been much in vogue notably in France with long duration of treatment.

By using surface applicators and interposing screens it is possible to obtain action at a depth without altering superficial tissue. By this filtration one diminishes the sum total of the rays considerably, necessitating prolonged exposures—50 to 200 hours. The very penetrating rays (passing through a screen of lead and rubber 1.28 m.m. thick) are called in Paris the 'hard beta' and the 'gamma rays,' the lead filter having absorbed the α , soft β , and 'medium' β rays.

One may combine use of 2 or more applicators around a tumour. This 'crossed fire' effect is very great, hence length of applying is reduced, and results in many cases are superior to those produced by γ rays. Various cases of carcinoma healed.—Wickham and Degrais, B.M.J. i./09,610,912.

The deeply penetrating γ rays after filtration, found hopeful for secondary gland lesions of cancer hitherto untreatable. Pharmacological experiments conducted on a frog's heart, applying radiation from 16 mgr. pure Radium Bromide, showed no effect. The same applied to the skin in the same time would have caused a severe burn.—R. B. Wild.

NEOPLASMATA of the skin, treated by Radium and "X" rays. Less than 1 hour doses of 5 mgr. per square cm. unsatisfactory. In most superficial cases screening is not necessary.—A. A. Russell Green, L. i./17,544.

TUBERCULOUS ADENITIS treated. Properly used a safe and certain cure. 15 mgr. spread on a flat circular applicator $1\frac{1}{2}$ in. in diam. is best. Screen of silver 1 mm. 10 hours is a suitable time for each application. Probably complete cure.—E. S. Molyneux, B.M.J. ii./19,705.

Cases treated in 1913/14 show no signs of recurrence. Square flat applicators used. Convenient size is 2 cm. sq. containing 15 mgr. of Radium Bromide (sometimes larger, viz. 1 square inch, containing the same amount). The Radium is in a cement not liable to damage. The plaque is screened with 1 mm. of Silver, then lint, then two layers of thin gutta percha tissue. The γ rays are used for the work. The screen absorbs the α and 99.9% of the β . Secondary β rays are set up on emerging through the Silver. The lint and gutta percha tissue absorb these. Dosage: twice a week at first, and later once a week, when the glands are subsiding.—E. S. Molyneux, L. ii./22,804.

CANCER has been treated at **Middlesex Hospital** with large quantities of Radium at a time. It has been a matter of speculation whether clinical results of exposing a tumour to small quantities, say, 1/5th Gm. for a certain number of hours would be improved if the intensity were increased 25 times (i.e. 5 Gm.), the time being correspondingly reduced. Hitherto the difficulty has been to obtain a sufficiently intense source of gamma radiation. This is now available.—L. i./20,164.

MALIGNANT DISEASE, EXOPHTHALMIC GOITRE, SPLENO-MEDULLARY LEUKAEMIA, HODGKIN'S DISEASE, KELOIDS AND NAEVI, treated at **Edinburgh Royal Infirmary**. Small rodent ulcers not affecting mucous membrane or bone are easily cured by 500 to 800 milligramme-hours, using a filter of Silver $1\frac{1}{2}$ mm. thick. In early malignant affections of the cervix, big doses, 6,000 to 10,000 mgr.-hours, should be given. In exophthalmic goitre, not much change can be expected in the size of the thyroid or in the exophthalmos, except in early cases, but if radiation consistent successful. Dose: 300 to 500 mgr.-hours, properly screened.—Dawson Turner, B.M.J. i./23,464.

The radiations emitted by the later disintegration products of Radium.—W. H. Brown and J. P. McHutchinson, Na., Feb. 23/24; P.J. i./24,222.

SKIN AFFECTIONS.—The later disintegration products of Radium, Radium D and E used, extracted by means of boiling Aqua Regia from finished Emanation Tubes. Formula for **Celluloid Varnish** used to fix active powder to Applicators. Solution of Celluloid in Amyl Acetate $\frac{1}{8}$ oz., Acetone $\frac{3}{4}$ oz., Acetic Acid $\frac{1}{4}$ oz., Acetic Ether $\frac{1}{8}$ oz. Used in lupus erythematosus and various types of naevi. Eczema and psoriasis also respond, but it was not

found convenient to treat large affected areas by means of application. The radiation in question has the unique property that it is absorbed by the part in question, since its effective penetration is only about 3 mm. of tissue.—J. P. McHutchinson and W. H. Brown, L. i./26,755.

Dosage in Radium Therapy.—B.M.J. i./29,506.

Dual Radio-therapy in malignant disease.

There may be some unknown factor in Radium radiations which, apart from their high degree of penetration, may account for their therapeutic effect.

The dual method for deep therapy is virtually a **combined cross-fire**; by working two tubes at the same time from both sides of the body a larger dose is given to the deeper pathological cells, and a large area is covered. Maximum dose used 20 X, through 3 mm. of Aluminium. Intrathoracic growth responded more rapidly than with the localised method used previously.—S. Gilbert Scott, B.M.J. i./21,771.

After-effects of Radium Treatment.

Radium (Mesothorium) necrosis.—An occupational disease among workmen employed at a Radium plant engaged in making luminous watch dials—four deaths recorded. It is, apparently, the result of introducing minute quantities into the mouth through the habit of pencilling the point of the brush with the lips.—F. L. Hoffmann, Jl. A.M.A., ii./25,961-5. The clock and watch industry of the U.S. is very large. Until the causative element is finally established and a reliable measure of dealing with it is found, every operator is exposed to uncontrollable danger.—*ibid.*, J. P. P. Knief. Some unrecognised dangers in the use of radio-active substances.—H. S. Martland *ibid.* ii./25,1769-1776.

Methods for the detection of radio-activity in the human body due to ingestion of radium, *e.g.*, in the manufacture of luminous watch dials.—H. S. Martland Jl. A.M.A. i./29,555.

Leukæmia following the use of radio-active substances. Produced through small doses frequently repeated over a long period.—Jl. A.M.A., ii./25,1571.

Untoward sequels are excessive skin reactions, fibrosis of deep tissue, increased pain, and mental or physical changes. An overdose externally may cause telangiectasis, scarring, and loss of hair. In uterine cases pain sometimes occurs in the hips, groin, back of leg, and in the lumbar spine. The mental after-effects are at present undetermined.—P. C. Fenwick B.M.J. i./29 473.

Henrique's method of reducing high blood pressure.—The method consists of the application of 50 mg. of Radium to each side of the skull at a point just in front of and a little above the external auditory meatus. The Radium is filtered by 2 mm. of brass and is at a distance of 1 inch from the skin. One hour's application is repeated weekly till pressure falls to normal. Relief of high pressure and attendant conditions, *e.g.*, intense headache, cedema of lower extremities, auricular fibrillation and facial paralysis.—A. Henriques, Radiol. Review (American).

Radium Institute (London) Report for 1917.

Analysis of cases of epitheliomata of the mouth, tongue, fauces and œsophagus, carcinoma of uterus, of rectum, of bladder and of the breast. Results in treatment of sarcoma on the whole more satisfactory than those of any other form of malignant disease except rodent ulcer. Radium rays though affecting normal tissues to a much less extent than morbid tissues, do affect them—this is a hindrance to an unlimited increase in the amount of radiation employed. Exophthalmic goitre at first aggravated, but later all the symptoms ameliorated (6 to 8 weeks).—B.M.J. i./18,349. L. i./18,442.

(Manchester and District Radium Institute Report. All early rodent ulcers can be cured.—B.M.J. i./19,320. P.J. ii./16,530.)

Radium Institute Report for 1920.

Beta rays do not penetrate far, the hard being reduced to about 6% by 1 cm. of body tissue. These rays, unscreened, are used for epitheliomata, which tend to fungate and not to invade the tissue; for those that so tend, the soft rays are cut out, and medium and hard rays only used. The blood of workers at the Institute, after lengthy exposure to the rays, show drop in red cells and hæmoglobin. Leucopenia invariably occurs. WHITE CELLS frequently reduced to half. Protection called for. With regard to DOSAGE: cross-fire radiation advised for epitheliomata. Details of treatment of CARCINOMATA.

SARCOMATA, RODENT ULCER, BLOOD AFFECTIONS, as also of EXOPHTHALMIC GOITRE. It is stated that Tubercle bacilli in cultures are not killed by at least 100 hours' exposure to Radium rays, but shorter radiation thought to diminish vitality. The beneficial effect observed in lupus may be brought about in this way.—B.M.J. i./21,609.

Report for 1921.—Devoted to gynæcological conditions.—B.M.J. i./22,356

Report for 1922.

Devoted chiefly to CARCINOMA OF TONGUE, OESOPHAGUS AND RECTUM. Emanation tubes, in addition to irradiation of the whole lymphatic area, stated to be a great advance, especially in the case of the tongue. In the case of the oesophagus the position is disappointing. Carcinoma of the stomach is treated in three ways (a) by laparotomy and embedding tubes 24 hours (b) by irradiation by an oesophageal tube rather uncertain, (c) from outside. Re carcinoma of rectum the report is favourable, but the rectal mucosa is intolerant of irradiation.—B.M.J. i./23,297,301.

Fordyce's disease of the lips, epithelioma of lip, leukoplakia of the cheeks, and other affections. Review and abstract.—L. i./23,503.

Report for 1923.

MALIGNANT GOITRE. In advanced and inoperable cases, Radium treatment should most certainly be adopted.

ENLARGEMENT OF SPLEEN. Radium treatment specially indicated in splenomegaly, splenic anaemia—Banti's disease—spleno-medullary leukaemia.

TUBERCULOUS ADENITIS. It is probable that radiation of tuberculous glands weakens vitality of contained tubercle bacilli and enables their destruction to be more readily accomplished by the phagocytic cells. It further acts as a stimulus to the production of fibroblasts, with consequent development of an encircling, constricting and protective fibrosis.

LYMPHADENOMA. Usually exhibits an exceedingly favourable response to Radium Therapy.

LYMPHO-SARCOMATA. Spectacular results. Peculiarly susceptible to gamma radiation.—L. i./24,409,410.

From *A Clinical Index of Radium Therapy* (by A. E. Hayward Pinch.) (Published by the Radium Institute, London, 1925):—

It is now a general rule in Radium Therapy that whenever the burying of a tube in a growth is possible this method of treatment should be adopted, and the employment of many small tubes, which can be inserted rapidly with a minimum of disturbance and discomfort, is superseding the use of 1 or 2 large tubes, more equal and effective radiation being obtained.

In diseases of the thyroid, thymus, spleen and lymphatic system flat surface applicators are chiefly employed.

Remarkable improvement has been effected in arthritis deformans by the daily administration of 250 Cc. of a Radon solution of a strength 2 millicuries per litre.

The action of Radium on normal tissues and organs, and the skin reactions following treatment, are described in the work which includes 'Clinical aspects of the Research Department of the Institute,' by J. C. Mottram, and 'The evolution of the present-day technique of preparing Radium and Radon applicators,' by W. L. S. Alton.

No Radium Institute Reports have been issued since 1925 owing to pressure of work.

Report of the Radiological Committee of the Medical Research Council on the Medical Uses of Radium.—Leader, B.M.J. ii./24,1170. See also L. ii./24,1353.

Summary of Reports from Research Centres for 1925.—Technique for MENORRHAGIA does not require further research. Radium valuable therapeutically in myeloid and lymphoid leukaemia, but only of temporary benefit. No radical change in Radium therapy of malignant disease during last 5 years, but tendency to use numerous comparatively *small sources of Radium for long intervals* (7-10 days) in place of single intense sources for shorter times. In advanced cases of cancer of breast prevents ulceration of the recurrence and saves much pain; in early cases large doses caused tumours to disappear or retarded growth; results very encouraging with primary carcinoma of the ordinary type. Temporary good results in cancer

of œsophagus. Sarcoma of bone successfully treated. Of 178 cases of inoperable cancer of uterus, 120 had died not less than 1 year after treatment, 27 were apparently free from disease, and 31 were alive but not cured. 50-100 mg. Radium element introduced into cervical canal for 22-24 hours.—B.M.J. ii./26, 1137.

Summary of reports from research centres for 1927.—Med. Res. Council. Spec. Rept. Series No. 126.

Radium Containers in current use comprise **Tubes, Needles, Plaques and Cells.**

Tubes.—These are of Platinum, hermetically sealed, usually 1 mm. thick. Any additional screenage can be added by enclosing in capsule screens. A 10 mgr. tube has total length 20·7 mm., external diameter 2·95 mm., length 15 mm.

Needles are cylindrical, with an eyelet hole at the end and either a conical or triangular trocar point at the other. They are usually of Platinum, with a percentage of Iridium for strength, 10% for the body of the needle and 25% at the point. The thickness of wall varies between 0·5 and 1 mm. (See also Screens *infra*.) A number of these needles containing, e.g., 1 to 3 mgr., can be used by embedding and produce cross-fire effect. '*Linear Intensity*' is a new factor, conveying the intensity of radiation per unit of length of the needle. Some hold that 0·6 mgr. per cm. length of needle is a safe maximum. Standard dimensions are now in use, e.g., for a 1 mgr. Platinum needle: total length 26·5 mm., external diameter 1·6 mm., length of chamber 15 mm., eyelet 5 mm., point and screw 6·5 mm.

Needles can be converted into tubes for use in cavities, and into plaques for surface use, by means of suitable applicators.

Plaques.—For surface use, employing the soft β rays Monel metal containing about 67% Nickel, 28% Copper, and 5% other metals, is used. The Radium is spread in the shallow portion and fixed in position—over this is a face of the same metal 0·1 mm. thick. This absorbs approximately 50% of the primary β radiation. The apparatus is therefore durable and uniform and supercedes varnishes and Vulcanite. Monel plaques may be square, round, oblong or oval. 'Double strength' plaques contain 10 mgr. Radium element per sq. cm., 'Full strength' 5 mgr., and 'Half strength' 2·5 mgr.

Cells are similar to tubes, but generally without eyelet, and may be used for minute amounts for building up applicators of desired Radium content.

The term '**Applicator**' is now employed to cover various devices holding the container in therapeutic use.

Sheath Needles are similar to ordinary needles, but the points are screwed into the shaft and hence removable. One, two, or more, 'removable cells' may be inserted.

Flat Applicators for Needles are of Brass or German Silver. These have windows and are made for holding 2 to 6 needles.

Needle Introducers, Prostatic Applicators, Uterine Sounds and Applicators for Antrum, Rectal or Vaginal and Oesophageal use are also available.

Screens of Lead of various thicknesses are used, e.g., $1\frac{1}{4}$ mm. thick, covered with rubber allow only γ rays to pass.

Lead $\frac{1}{16}$ to $\frac{1}{2}$ m.m. permits the 'hard beta' rays as well as the gamma.

Silver 1 mm. absorbs 99.9% of the hard β rays and **Brass** 1.3 mm. absorbs that amount. When the aim is to utilise β rays, the duration is so relatively short that the γ ray effect is wanted. Screens are necessary to cut off the β rays, because of their greater action on the superficial structure.

Remembering, in dealing with effects of radiation on the deep structures, that from a point source the intensity of the radiation diminishes inversely as the square of the distance, and taking other figures into account, the physiological effect of the γ rays is limited to a distance of 2 to 3 cm. in the treatment of malignant disease, when the dose required to induce the disappearance of new growth is one which will almost produce a similar effect on adjacent normal tissue.—R. Knox, B.M.J. i./22,631.

Platinum $\frac{1}{2}$ mm. screens off 99.9 of the primary β and enables the use of all γ rays.

Gamma radiation acts by dissolution and absorption, while beta radiation acts by destruction through necrosis, with consequent suffering to the patient. The importance of adequate screening.—Sir C. Gordon-Watson and Stanford Cade L. i./29,634.

Radon (Radium Emanation).

The therapeutic effect of Radon (Radium Emanation) and Radium Salt are stated to be identical.—Report of Radium Inst., L. i./24,401.

MALIGNANT DISEASE OF THE UPPER AIR AND FOOD PASSAGES—Surgical removal of growth should be undertaken when practicable. The lymphatic nodes should be removed, and the lymphatic vessels between the growth and the infected nodes irradiated, preferably from within. Where possible, the growth to be irradiated should be exposed. The introduction of a number of seeds of emanation better than implantation of screened tubes. As the periphery of the growth is reached the emanation dose may be reduced, 10, 20, or even more seeds are buried. The seeds, from 3 to 6 mm. in length and 1 to 2 mm. in thickness, containing a dose of 0.5 to 1 mc. of emanation (=0.5 to 1 mg. Radium element) are implanted parallel 1 cm. apart, and become encapsuled or slough out. 1 mc. of emanation emits 132 hours of radioactivity.—Sir W. Milligan B.M.J. ii./26,825. Treatment by either method—the cases most suitable are those in which the growth is confined to the mouth.—W. S. Syme, B.M.J. ii./26,826.

Screened Radon Seeds for Implanting.

The seeds are cylindrical shells of Platinum tapered at both ends containing a piece of capillary glass tubing containing Radium emanation. Each seed is 6 mm. long and 1.1 mm. in diameter, with a wall of 0.3 mm. of Platinum. Attached to the seed is a fine black thread, which marks the position of the seed in the tumour and facilitates its removal. The seeds contain 1.5 millicuries of Radon at the time of implanting, giving 200 millicurie hours, radiation if left for 14 days. The Platinum screen allows about 90% of the gamma rays to pass through, with less than 5% of beta rays. A trocar with a special cannula is used for implanting the seeds, which are implanted about 2 cm. apart. While customary to remove seeds when period of activity is over, no ill-effects have been noted where seeds have been left permanently in the tissues. Encouraging results with tumours which are difficult to treat by other methods. The initial response is more rapid than with other forms of Radium therapy. The local reaction is brisk in some cases.—P. Gosse, and F. E. Chester-Williams, L. ii./28,323.

Wertheim's hysterectomy for advanced carcinoma of the cervix made possible by the use of Radium Emanation tubes buried in the cervix and surrounding tissues.—L. i./20,1270,1278.

Malignant granuloma of the nose well treated by Radium emanation. Four tubes of about 12 millicuries in steel needles wrapped in lead were left in 18 hours. A second dose of 20 millicuries was also given and a further dosage on recurrence.—Sir R. Woods, B.M.J. ii./21,65.

Some patients treated with no results with X-Rays and Radium recovered after a single application of Radon. Results better where no previous treatment had been applied and where the intratumoural method of treatment is applicable. The introduction of needles is advisable only where the tumour is sufficiently large and is not closely adjacent to the bone: best results in cancer of the tongue, lip, penis, and other similar organs, but the application of masks with Radon gave favourable results in other parts.—The average dose for superficial application or filtration through 2 mm. Lead is 1 to 1.5 mcd. (millicuries detruites—decomposed Radon) over 1 sq. cm. of surface, decreasing this for large areas (100 sq. cm. or more): for body cavities 1 to 3 mcd. per cm. of length (in cancer of the œsophagus): not more than 2 mcd. per cm.): intratumorally, 0.5 to 1 mcd. per cc. of the applied tissue. The Radon is usually left for 7 to 10 days.—M. I. Nemenow and F. S. Grossmann, B.J.R., June, '28, 187—196, July, '28, 245.

Radium Emanation Water.—*Dose.*—Half a pint a day six days a week for six weeks for patients suffering from rheumatic gout and similar affections were advised by the late Sir F. Treves. Two such courses generally effected a cure. This refers to the Radium Institute product which is stated to be 4,000 to 5,000 times stronger than Spa Waters.

Sea Water contains about, 0.9×10^{-12} Gm. Radium per litre, i.e. 1 billionth part of a gramme per litre, in the North Atlantic; various other sources yielded an average of 16×10^{-12} Gm. per litre,—the amount in River waters is less—e.g., about 1/4 that of the Atlantic for the St. Lawrence, and the Nile respectively. The amount in The Atlantic is said to be about 1/20 that in a weak radio-active spring.—S. Russ.

The Sea contains about 20,000 tons of Radium. One ton of Radium is equal to 1,500,000 tons of coal in energy. A Gm. of Radium gives off in its lifetime about 3,000 horse power.—C. E. S. Philips, Cancer Hospital Lecture, 10/12/13.

See also **Sea Water Injections**, Vol. I.

Dols Flannel described as of high radio-activity. For rheumatism, neuritis, bronchitis, lumbago, sciatica, stiffness, sore throat, sprains, etc.

Pitchblende Ointment.

Pitchblende 25% finely powdered in Soft Paraffin. In the palliative treatment of malignant growths.

Radium Ointment, Radium Salve.—Preparations under these names have been supplied commercially. Weak Radium Ointments, preferably made with a thoroughly dried soft paraffin basis, might prove of considerable utility in some cutaneous affections, e.g., in lupus, psoriasis, eczema, boils, ulcers, and ringworm.

Radio-active Mud.—Continental Spas with a reputation for treatment of rheumatic affections by mud baths owe their results probably to the fact that the mud is radio-active. Such mud can only be used at the source.

Uranium Mud or Actiniferous Earth is similar, it is understood to be the by-product formed during the process of breaking up uranium ores. Its radio-activity is said to be due to traces of Radium, Polonium, and in particular to Actinium. It emits emanation of low activity.

Rheumatic arthritis, gonococcal rheumatism, nerve affections and skin diseases have been treated by compresses and pads of the mud, or in baths, about 8 ounces to 40 gallons of warm water. The length of application of pads varies with the case—it may be several hours.

Radio-active mud from wells in Pistany, Czecho-Slovakia, for making into poultices.—L. ii./22,744.

The therapeutic action of mud baths.—E. Duhot, Paris Med., Apl. 18, '25, 345, per Pres., Mar., '26, 134.

Radio-Synthesis.—It is possible to form organic chemical compounds from the moisture and Carbon Dioxide in the atmosphere by the aid of Radium.—Na. 1922, p. 714.

Potassium and Rubidium emit β rays but show no other evidence of radio-activity.

RADIO-ACTIVE DISINTEGRATION PRODUCTS OF THORIUM.

Thorium Nitrate, described in Vol. I., (used for gas mantles) and Mesothorium, are obtained from Monazite Sand. Travancore, in the extreme South of India, is a source of origin, as also Brazil. The sand contains 5% to 7% ThO_2 , 25% to 30% Pb_2O_5 , 25% to 35% Ce_2O_3 and 20% to 30% La_2O_3 , Pr_2O_3 and NdO_3 . Titanium White, a Titanite of Iron, is obtained in working. It is used as a paint for interiors—it is innocuous and does not blacken in town air. Mesothorium yield from the raw material is 6 to 7 mgr. per ton. Process described. Its activity is reduced to half in 4 or 5 years.—E. White, P.J. ii./22,440 ; C.D., Nov. 11, 1922, p. 671.

Thorium changes, broadly speaking, into Mesothorium, and this to Radiothorium, and this to Thorium X, and this to a series of other products. The following are the disintegration data as to Thorium (*cf.* Radium chapter).

Thorium shows an activity, measured by α rays, about the same as pure Uranium compounds, but the β and γ ray activity is feebler. In the by-products of a single year's manufacture of Thorium for the mantle industry the Mesothorium and Radiothorium capable of being extracted possess, it has been stated, as much radio-activity as at least an ounce of pure Radium.

Thorium 'X' is prepared from pure Thorium Salts (which always contain Radiothorium, the immediate parent, in considerable amount). It is obtained by addition of Ammonia to a Solution of a Thorium Salt, and evaporating the filtrate and removal by ignition of the Ammonium Salts. It is transformed directly into emanation so that the rate of production of emanation is directly proportional to the amount of Thorium 'X.' About a month after removal of Thorium 'X' the Thorium regains its original activity and shows an α ray activity equal to about one-quarter of its value before separation. This was at first thought to be the activity due to Thorium itself, but later work has shown that this residual activity is due in part to unseparated products. After separating the thorium from the Ceylon mineral Thorianite which yields large quantities of helium, Hahn found a radio-active substance of slow rate of transformation in the residues which gave rise to Thorium X, and the Thorium emanation—Radiothorium.

Radiothorium is not separable from Thorium by any chemical processes. Hahn found that other radio-active products must be present in thorium. On examining commercial preparations of Thorium of known ages, it was found that the α ray activity of Thorium after separation decreased at first for some years, passed through a minimum, and then slowly increased again to a final value represented by the activity of a pure Thorium compound, from which none of the radio-active constituents had been separated. To explain this it was necessary to assume the existence of another

THORIUM

from the International Tables

T	$\theta = \frac{1}{\lambda}$	λ (sec.) ⁻¹	Name	Symbol	Atc WT.
1.31 × 10 ¹⁰ yrs 6.7 yrs.	1.89 × 10 ¹⁰ yrs 9.67 yrs.	1.68 × 10 ⁻¹⁸ 3.28 × 10 ⁻⁹	<i>Thorium</i> <i>Mesothorium 1</i>	Th MsTh1	232 228
6.2 hours	8.9 hours	3.12 × 10 ⁻⁵	<i>Mesothorium 2</i>	MsTh2	228
2.02 yrs.	2.91 yrs.	1.09 × 10 ⁻⁸	<i>Radiothorium</i>	RdTh	228
3.64 days 54 secs.	5.25 days 78 secs.	2.20 × 10 ⁻⁶ 0.0123	<i>Thorium X</i> <i>Thoron</i>	ThX Tn	224 220
0.14 sec.	0.20 sec.	5.0	<i>Thorium A</i>	ThA	216
10.6 hours	15.3 hours	1.82 × 10 ⁻⁵	<i>Thorium B</i>	ThB	212
60 mins.	87 mins.	1.92 × 10 ⁻⁴ [1.25 × 10 ⁻⁴]	<i>Thorium C</i> —	ThC	212
10 ⁻¹¹ sec.	10 ⁻¹¹ sec.	10 ¹¹ (?)	<i>Thorium C'</i> <i>Thorium Ω'</i> (Lead)	Th C' Th Ω' Pb ²⁰⁸	212 208
.....	[6.7 × 10 ⁻⁵]	<i>Thorium C</i> —	ThC	212
3.1 mins.	4.5 mins.	3.70 × 10 ⁻³	<i>Thorium C''</i> <i>Thorium Ω''</i> (Lead)	ThC'' Th Ω'' Pb ²⁰³	208 208
.....

Note 1.—Thorium. The value given for λ is that obtained from the direct counting of the α -particles emitted by a compound of thorium. All the other values are less; the smallest being 0.55 of that given in the table and giving for $\theta = 3.45 \times 10^{10}$ years and for $T = 2.37 \times 10^{10}$ years (*Phys. Zeits.* 1918, 19, 259).

Note 2.—Thoron is also called the thorium emanation.

Note 3.—Thorium C undergoes a double disintegration: 65% of the atoms emit β -rays and produce the substance ThC' which gives

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Radioactive Elements—1923.

Radia- tion	α_0	V	$\mu_{\beta}\text{Al}$	$\mu_{\gamma}\text{Al}$	$\mu_{\gamma}\text{Pb}$	Notes
α	2.58	0.0469	1
—
and γ	$\left\{ \begin{array}{l} 0.37; 0.39; \\ 0.43; 0.50; \\ 0.57; 0.60; \\ 0.66 \text{ and } > \\ 0.70 \end{array} \right\}$	20.2 to 38.5	26; 0.116	0.62
α (β)	3.67	$\left\{ \begin{array}{l} \alpha 0.0527; \\ \beta 0.47; 0.51 \end{array} \right\}$
α	4.08	0.0546
α	4.74	0.0574	2
α	5.40	0.0600
and γ	0.63; 0.72	110	160; 32; 0.36
35% β	$\left\{ \begin{array}{l} (\text{C} + \text{C}'') 0.29; \\ 0.36; \\ 0.93 \text{ to } 0.95 \end{array} \right\}$	14.4	3
α	8.16	0.0688
.....
35% α	$\left\{ \begin{array}{l} 4.55 \\ 74.69 \end{array} \right\}$	0.0572	4
and γ	(See ThC)	21.6	0.096	0.46	5
.....

ys, and 35% emit α -rays and produce the substance ThC'' which
s β -rays.

ote 4.—*Thorium C*. The value $\alpha_0=4.69$ is that corresponding
V=0.0572 which has been directly measured.

ote 5.—*Thorium C''* is also called thorium D.

or the meaning of the symbols T, α_0 , V, etc., see the data
the Uranium, Radium and Actinium series, p. 327.

product in Thorium called Mesothorium which had been produced from Thorium and was transformed into Radiothorium.

Mesothorium is easily separated from Thorium. There is no doubt that the initial discovery of Radiothorium in the Thorium residues was not a result of the separation of Radiothorium directly from the Thorium, but of the separation of Radiothorium which had grown in the interval from Mesothorium. A day after separation a preparation of Mesothorium shows a strong β and γ ray activity.—Sir E. Rutherford.

Sir E. Rutherford stated that as a large amount of Thorium is being continually separated for the mantle industry the activity of the Mesothorium capable of separation is very great, and there seems to be no reason why an amount of Mesothorium equivalent in β and γ ray activity to several grams of radium should not be produced annually.

Commercial Mesothorium is standardised by comparing the ray activity with that of a standard Radium preparation.

A, β and γ ray activity in a specimen of Mesothorium initially equal to one milligram of radium will increase in three years to the equivalent of 1.5 milligrams, and after ten years will again be equal to one milligram. Consequently during this ten years it has an average activity equal to 1.2 milligrams of Radium. It will ultimately decay to about half the initial value after twenty years. See also previous Edns.

Mesothorium was at first believed to emit β rays, but later work has shown that this is due to the presence of a substance of quick period, which is produced by the Mesothorium. This new product called Mesothorium 2 emits only β rays, and has a half value period of 6.2 hours, as stated in the Table.

To test Radium for Mesothorium.—The simplest test is to heat it for a short time to drive off the emanation. The preparation must then lose its γ -radiating power after a few hours, completely regaining it only after the lapse of many weeks. Instead of heating it, it can of course be dissolved in water and the solution evaporated. If after the radium emanation has been driven off, and the radium C has been destroyed (which takes a few hours) there is still some γ -radiation, this is due to mesothorium. The ratio of the γ -radiation before and after the treatment is a measure of the proportion of Radium and Mesothorium in a mixture.—*Berichte* xliii., 3240. *Chemical News*, Jan. 13, 1911. *J.R.S.*, April, 1911. *J.C.S.A.* ii./11, 8.

The chemical similarity of Radium and Mesothorium forms an example of two elements of different radioactivity but *entirely identical* chemical character. The **process of extraction** of Mesothorium from Monazite residue is similar in principle to that of Radium from Pitch-blende residues.

Mesothorium and Radiothorium produce very marked effects on a Zinc Sulphide Screen.

Ratio of Mesothorium to Thorium.—R. N. McCoy and L. M. Henderson (*Abst.*), *J.R.S.*, Apl. '19, p. 62.

Therapeutic Use of Thorium Degradation Products.

Thorium Salts are poisonous if introduced in the system.

Mesothorium. Action on malignant growths is said to be 'just like Radium.' Cancer of the tongue showed improvement. Psoriasis plaques are recorded to have been cured.—See also L. i./14, 418.

Malignant and non-malignant cases treated by introduction of Mesothorium into the uterus in capsules.—*B.M.J.* ii./13, 923, but burns have been caused by its use.

Thorium 'X.'—Has been injected into sarcomata and given intravenously in dose (?) of 1/100,000 mgr. in 1 Cc. of Normal Saline, but is dangerous and must be used with caution.

Myeloid leukaemia treated with Thorium "X" intravenously, commencing with 50 electrostatic units and increasing the amount. Treatment continued for 9 months, during which 8,000 electrostatic units were given. The dose must be found experimentally in each case, the blood condition being an indication of amount required.—B.M.J.E. ii./24,41. *Numerous further abstracts on the subject, last Edn., p. 341,342.*

Thorium 'X' Poisoning has occurred from injections.

Thorium emanation.—Inhalations may be effective in the initial stage of chronic rheumatism. Three patients took daily inhalations, for 15 to 30 days, of 70 to 90 units. Treatment of no value in subacute and contra-indicated in acute form. In cases with exostoses intramuscular injections of Thorium-X are preferred.—per Jl. A.M.A. ii./25,153.

URANIUM.

U=238.17

Scientifically, this Chapter should of course have preceded Radium, but for ease of reference it is placed alphabetically.

Uranium is a constituent of Pitchblende (v. Radium Chapter) to the extent of 40 to 70%. Carnotite, a hydrated Potassium-Uranium-Vanadate, a yellow mineral found as specks in sandstone or as incrustation in the cracks of this in Western Colorado, is a source of Radium.

Uranii Acetas. $\text{UO}_2(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O} = 424.25$

Small yellow crystals with odour of Acetic Acid.

Employed principally in chemical analysis, *e.g.*, Estimation of Phosphoric Acid, *cf.* Urine Analysis.

Luminosity of Uranium.

Metallic Uranium and its salts shaken in a bottle give brilliant yellowish-white glow. The luminosity can be maintained by continued shaking, and the general illumination seen easily throughout a large room. The Nitrate and Yellow Oxide showed the same effect, but to a very much smaller degree, whilst the Black Oxide and Sodium Uranate do not give it.—Na., Dec. 15/10, 207.

The effect is due to oxidation of minute particles which are knocked off. The sparks in question will explode a mixture of Hydrogen and Oxygen or ignite Petrol for an engine.—Na., Jan. 1911, 308.

Uranium-Calcium Phosphate (Hydrated). *Syn.* AUTUNITE (from Autun in France). $\text{Ca}(\text{UO}_2)_2(\text{PO}_4)_2 \cdot 8\text{H}_2\text{O}$.

This yellow mineral has been used for irradiating diseased tissues and for treating chronic deafness, but it seems probable its effects are too weak. To determine utility exposure for three hours in the dark should provide visible radio-active effect on a photographic plate. It should produce a shadowgraph of a coin in 6 hours, if the coin be placed on the plate, then a piece of wood 1 inch thick and the mineral above it must contain at least 50% of the crystals in the matrix.

Uranium Copper Phosphate is URANITE (*Syn.* Cuprouranite or Torbernite.) The crystals of this are vivid green, and are found in Cornwall.

URANIUM 'X'

URANIUM AND ITS DISINTEGRATION PRODUCTS.

It was shown by Sir William Crookes and M. Becquerel that from Uranium Salts, by chemical processes, a small amount of substance (then called Uranium X), could be isolated, which was responsible for the whole of the β -ray activity. The salts freed from this Uranium X gradually and completely recovered their power of producing β -rays, so that the Uranium X was formed by the decomposition of Uranium.

It has since been found that the disintegration is rather more complex, Uranium X itself not being a simple substance. By loss of a Helium atom (α ray) Uranium I (238) is converted to Uranium X₁ (234), which has a half-life value of 24.6 days. This gives rise to β rays, changing to Uranium X₂ (234), also called Brevium, which has a period of only 1.15 minutes, a further loss of β rays giving Uranium II. This is related to Radium through Polonium, and it seems probable that either Uranium I or Uranium II gives a branch chain containing the Actinium series.

For further data regarding the products of Uranium see the table for the Uranium and Radium series, *antea*.

Uranii Nitras $[\text{UO}_2](\text{NO}_3)_2 + 6\text{H}_2\text{O} = 502.282$.

Dose.— $\frac{1}{2}$ to 5 grains (0.03 to 0.3 Gm.) after meals.

Lemon-yellow prismatic crystals. Soluble in water 2 in 1. Taste astringent.

In psoriasis and senile atrophy of the skin, lotion of this salt 20 grains to the ounce useful and Uranium Oxide Ointment (*q.v.*).—A. Clark, B.M.J. ii./12,716.

Uranium Oxide occurs in 2 forms:—

(1). Uranous Oxide. *Syn.* Uranium Dioxide $\text{UO}_2 = 270.17$.

A black powder soluble in Nitric Acid.

(2). Uronic Oxide. *Syn.* Uranium Trioxide $\text{UO}_3 = 286.17$.

Orange yellow coloured powder soluble in mineral acids.

Uranium Trioxide as dusting powder in a recurrent case of carcinoma after surgical treatment. In lupus erythema as ointment 1 to 3 of Lanolin. Also 15 grains of the yellow Oxide in Sterile Oil injected into the substance of malignant growths.—A. Clark, B.M.J. ii./12,716.

Experimental nephritis produced by Uranium Nitrate.—L. i./14,1453.

Uranii et Quinlnæ Chloridum.

Dose.—3 to 6 grains (0.2 to 0.4 Gm.) thrice daily.

Yellow crystals, soluble 1 in 100 of water. For diabetes and gout.

Uranii Oleas. *Dose*.— $\frac{1}{2}$ to 5 grains, *vide* Oleata, Vol. I.**Uranii Salicylas.** *Dose*.—5 to 20 grains (0.3 to 1.2 Gm.).

In reddish powder, is better tolerated than the nitrate.

Acidum Molybdicum $\text{H}_2\text{MoO}_4 = 162.016$.

May be prepared by precipitating from a solution of a Molybdate, *e.g.*, Sodium Molybdate with Hydrochloric Acid. It is soluble in excess of the Acid. White crystalline powder. Its employment is chiefly technical and analytical. Ammonium Molybdate is contained in Froehde's Reagent, *q.v.*, used for testing for Alkaloids.

ANALYTICAL MEMORANDA.

CHEMICAL TESTS & MICROSCOPIC METHODS for
THE EXAMINATION OF URINE, BLOOD, FÆCES, &c.

URINE.

The quantity of urine is increased in chronic interstitial nephritis, diabetes insipidus and diabetes mellitus. It is decreased in severe diarrhœa, fevers, uræmia and conditions which interfere with the circulation through the kidneys. The usual yellow colour is due to pigments *e.g.*, urochrome. Blood pigment gives a red or brown, smoky colour. Urine which changes to a red colour on adding alkali is sometimes passed by patients taking phenophthalein. Dark black urine suggests alkaptonuria, melanotic tumours or phenol poisoning.

The normal reaction is slightly acid (pH 6·0), due partly to acid phosphates and partly to free organic acids. Urine may become slightly alkaline after a full meal. On standing it becomes alkaline owing to decomposition of urea and formation of ammonia. A similar marked alkalinity of freshly voided urine may be due to ammoniacal decomposition occurring in a severe case of chronic cystitis.

The Specific Gravity of urine at 60° F. is usually between 1·015 and 1·025. It is low in chronic interstitial nephritis, diabetes insipidus and many functional nervous disorders. It is high in fevers, parenchymatous disease of the kidney and diabetes mellitus.

The Total Solids of the urine of a healthy adult amount to about 60 grams or 950 grains per diem. A quick clinical method of determining the total solids is to multiply the last two figures of the specific gravity by the number of ounces voided and add one-tenth of itself. This gives the amount in grains, *e.g.*, $45 \times 20 = 900 + 90 = 990$ grains.

The specimen to be examined should always be the first urine passed on waking in the morning. In female patients care is necessary in the collecting of the specimen and in a doubtful case of pyuria a catheter specimen is preferable.

Microscopic Examination.

The chief objects to be sought for are blood, pus, epithelium, casts, chemical deposits (crystalline or amorphous) and parasites. The centrifuged deposit or sediment should be used ; a drop on slide is covered with a cover slip and studied with a 2/3 and 1/6 inch objective. For accurate estimation of red blood cells or pus the cells in the fresh uncentrifuged urine should be counted in a Fuchs Rosenthal cerebro-spinal fluid counting chamber. *Blood dealt with on p. 391. Casts and Pus are in alphabetical position.*

Epithelium.

Epithelial cells are normally present and have no pathological significance. They are larger than pus cells, rarely round, usually non-granular and with a small central nucleus. It is impossible to determine the region of the urinary tract from which epithelial cells have been derived, but a rough classification may be made.

Angular squamous epithelium comes from the vagina. Cells from the ureter or pelvis of the kidney are small and round, resembling polymorphonuclear leucocytes except that their nuclei are definitely round. Such cells are commonly seen in specimens collected by ureteric catheterisation and must be distinguished from pus corpuscles. Fragments of tumours of the urinary tract should be teased out and stained, or, better, cut into microscopic sections. The recognition of isolated cells from a neoplasm is impossible.

Chemical Deposits.

The detection of a crystalline or amorphous deposit in the urine is no evidence that this substance is being excreted in excess, and in a case of calculus the chemical composition of the urinary sediment gives no indication of the nature of the stone.

The only urinary deposits likely to be found in **acid urine** are **Urates, Uric Acid, Calcium Oxalate, Stellar Phosphates** and **Cystin**. Urates are amorphous, brown or pink and disappear on warming, Uric acid appears in many different forms as yellow or brown crystals which are soluble in sodium hydroxide and reprecipitated by hydrochloric acid. Calcium oxalate occurs as clear colourless octahedral crystals with an envelope appearance, or as dumb bells. They are insoluble in acetic acid but readily soluble in hydrochloric acid. Stellar phosphates are composed of calcium hydrogen phosphate and are readily soluble in acids. They appear when the urine is nearly neutral. They form long narrow flat prisms which are frequently collected in bunches or rosettes, or may be fine and feathery. Cystin occurs only in patients with the rare congenital abnormality of **CYSTINURIA**. They occur as irregular hexagons with clear-cut straight sides. The crystals are insoluble in acetic acid and ether, but soluble in hydrochloric acid and in ammonia and other alkalies. They occur only in acid urine.

The commonest deposits in **alkaline urine** are **Ammonium Urate, Amorphous Phosphates, Triple Phosphates** and **Calcium Carbonate**. Stellar Phosphates occur sometimes, Ammonium urate forms a brownish deposit, soluble on warming. Amorphous phosphates form a white amorphous deposit, soluble in acids. Triple phosphates form clear colourless crystals of various shapes and sizes, the typical ones being shaped like a knife rest. They are soluble in acids. Calcium carbonate forms a white deposit which may be amorphous or crystalline, of dumb bell shape. It dissolves in acid with effervescence.

In cases of **ACUTE LIVER ATROPHY** leucin and tyrosin may be found in the urine. Leucin crystals appear as yellow spheroids with radial and concentric striations, soluble in acids and alkalies. Tyrosin forms brush-like tufts of fine needles which are soluble in ammonia and hydrochloric acid and insoluble in acetic acid.

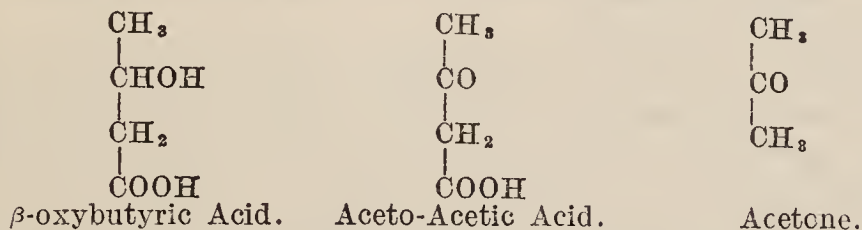
Parasites.

The only pathogenic parasites likely to be found in the urine are the ova of *schistosoma hæmatobium*. When **HÆMATURIA** is present the ova are usually numerous, appearing as large oval bodies with a definite capsule terminating in a single sharp spine. If the ova are scanty the patient should be told to empty his bladder and then to pass the last few drops of urine, evacuated by active straining, into another receptacle.

The following are dealt with in approximately alphabetical order.

Acetone and Allied Bodies.

The ketone bodies which often form abnormal urinary constituents comprise Acetone, Aceto-Acetic Acid and β -oxy-butyric Acid. Their presence is usually due to the incomplete metabolism of fat, as for example when the tissues are deprived of carbohydrate. The chemical relationship between them is shown thus:—



Quite probably β -oxybutyric Acid and Diacetic Acid are normally formed in the body during the splitting up of fat, but they are then fully oxidised.

It may be observed that the clinical significance of either Aceto-Acetic Acid or Acetone (β -oxybutyric Acid is not usually tested for) is the same.

Tests for Acetone Bodies.

Gerhardt's Test consists of adding Ferric Chloride Solution 10% drop by drop to the urine. At first a precipitate of ferric phosphate appears which redissolves in excess of the reagent. If Aceto-Acetic Acid *Syn.* DIACETIC ACID, $\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{COOH} = 102\cdot048$ be present in concentration of 0.07% or over the solution turns a Bordeaux red colour. The colour should be compared with that obtained by adding ferric chloride to normal urine. A positive reaction indicates a severe degree of ketosis but a negative reaction does not signify that the patient is free from the dangers of ketosis. This is partly owing to the relative insensibility of the reaction and partly owing to the fact that Aceto-Acetic Acid is converted on standing into acetone, which does not respond to Gerhardt's test. Various drugs cause a similar colouration with ferric chloride, but such fallacies are easily overcome by boiling another sample of the urine prior to testing. If the colour be due to Aceto-Acetic Acid a negative reaction will be given by the boiled urine because the acid is volatile. The colour due to drug derivatives on the other hand is not effected by previous boiling of the urine.

Rothera's Test for Acetone and Aceto-Acetic Acid is a much more delicate test for ketosis. About 20 Cc. of urine should be saturated with ammonium sulphate and a few drops added of a freshly prepared dilute solution of Sodium Nitro-prusside, $\text{Na}_4\text{Fe}_2(\text{CN})_{10}(\text{NO})_2 + 4\text{H}_2\text{O} = 595\cdot828$ (soluble 1 in $2\frac{1}{2}$). 2 or 3 drops of 10% ammonia are added and the tube shaken. If the reaction is positive a delicate permanganate tinge develops which gradually deepens. A brown colour does not constitute a positive reaction. **Legal's Test** is similar. The Nitroprusside is added to the specimen or a distillate made slightly alkaline with potash. A red color,

changing rapidly to yellow is positive. Acetic Acid added gives reddish violet changing to blue.

The amount of Aceto-Acetic Acid can be judged by the depth of the colour and the rapidity with which it develops. A quick strong reaction corresponds to 0.25% and a slow weak reaction to 0.0005%. Intermediate reactions indicate proportional concentrations of Aceto-Acetic Acid.—(Kennaway.) There are no fallacies in Rothera's test. A faintly positive Rothera's test is not of such grave importance as a positive Gerhardt's reaction.

* "Endolytic Tubes" (cf., p. 364 and Glucose Tests) are made containing Sodium Nitro-prusside and Ammonium Chloride to be used in conjunction with a little washing soda or Liquor Potassæ, and also of Ferric Chloride.

A large drop of urine is taken on a sheet of notepaper and saturated with a crystal of soda. The saturated urine is allowed to run up a tube, the reagent having been shaken to the lower end. If Acetone is present in quantity a petunia colour develops in about 30 seconds, and even with small amounts a rosy or amethyst flush is noticeable in a minute or two. When absent, the powder dissolves with a pale straw coloration.—M. Fawkes, B.M.J. i./25,24.

Iodoform Test.—Distil the sample and make distillate alkaline with potash, add a little iodine solution (not an alcoholic solution). The formation of iodoform, recognised by yellow turbidity and the odour, indicates presence of acetone. *Microscopic Examination* is more conclusive than the odour.

Determination of Acetone in Urine—formation of Iodoform in the usual way and converting this into Silver Iodide and weighing.—Y.B.P. 1919, 5.

Scott-Wilson Test.—Place one drop of Scott-Wilson Reagent (*q.v.*) on a microscopic slide and invert slide to form a hanging drop. Place the slide over the mouth of a flask containing the urine or blood and leave for 2 minutes. If Acetone is present, the drop shows a fine white clouding or precipitate. A rough estimation of the amount of Acetone present may be obtained as follows:—

Faint trace	Opalescence	0.005%
Trace	Faint turbidity	0.01%
Moderate trace	Turbid	0.025%
Heavy trace	More marked	0.05%
Moderate amount	Very marked	0.075%
Large amount	Precipitate	0.1%

Compare by setting up a series of tubes containing Acetone from 0.1% down to 0.005%.—A. Wallhauser, J.L. A.M.A. ii./28,21.

Testing Expired Air for Acetone.

Moisten a watch-glass with Scott-Wilson Reagent and hold close to patient's mouth and nose for 2 or more minutes. Acetone reaction shown by clouding of the reagent. Of practical value in the differential diagnosis of the unconscious state, e.g. diabetic coma.—A. Wallhauser, J.L. A.M.A. ii./28,21.

Riegler's Test.—Differentiates Acetone and Aceto-Acetic Acid in urine. 10 Cc. of the specimen are acidified with 5 drops of 30% Acetic Acid and 5 drops of Lugol's Iodine solution are added. Shake out with 2 to 3 Cc. of Chloroform. No colour appears if Aceto-Acetic Acid be present. The Iodine is absorbed by the Aceto-Acetic Acid forming a colourless compound.

Hurtley's Test for Aceto-Acetic Acid.

To 10 Cc. of urine add 2.5 Cc. of Concentrated Hydrochloric Acid and 1 Cc. 1% Sodium Nitrite. Shake and allow to stand two minutes. Add 15 Cc. of strong Ammonia followed by 5 Cc. of 10% Ferrous Sulphate or a solution of Ferrous Chloride of equivalent strength.

2 Gm. Fe in 100 Cc.). Shake and pour into a 50 Cc. Nessler glass. Do not filter. Violet colour forms slowly.

Acetone does not respond to the test.—It is exceedingly delicate. It is assumed that iso-nitroso-acetone is first formed which then colours with the ferrous sulphate. The test can be rendered quantitative colorimetrically. As much as 0.4% has been found.

Colorimetric method for the determining of acetone bodies in blood, based on a reaction with Salicylaldehyde.—Y.B.P., '27, 93.

The Acetone content of the blood is 43.5% higher in pregnant than in non-pregnant women. During the second stage of pregnancy it reaches 12 mg. per 100 Cc. of blood, returning to normal shortly after delivery.—per JI. A.M.A. 1/25, 861.

The limiting concentration in Legal's Test is, for Aceto-Acetic Acid, 6 mgr. per litre, and for Acetone 100 mgr. per litre.—J.C.S., 1925, Ai.1490.

Iodine Absorption Test, Bela and Ondrovich.—5 drops of Acetic Acid 10% are added to 5 Cc. of Urine, then 1 drop of 1 in 500 Methylene Blue or .s., to give blue tint. Then titrate with N/10 Iodine Solution until a red tint appears.— $2I = CH_3CO.CH_2COOH$.

Iodic Acid Test.—Add to 1 or 2 Cc. of normal urine 2 Cc. of 10% Iodic Acid Solution and 3 Cc. Chloroform. Uric Acid, etc., reduce the Iodic Acid—the Chloroform becoming coloured with the Iodine. Now add 10 cc. of the specimen to be tested and shake thoroughly. If Aceto-Acetic Acid present the colour disappears, if absent it is intensified.

Hydroxy- or β -Oxy-Butyric Acid $CH_3CHOH.CH_2COOH$ may be extracted from the specimen with ether, and gives a reddish-violet colour with Ferric Chloride—the diacetic acid gives approximate index of the content of this acid. It occurs only if Diacetic Acid be also present. The specimen may be fermented to remove sugar, precipitated with lead acetate and ammonia; if the filtrate be laevorotatory β -Oxy-Butyric Acid is probably present.

Sellard's Test for Acidosis in diabetes. *Suggested by MacLean.* This depends on the ability of a normal individual to secrete an alkaline urine after taking 5 to 10 Gm. of Sodium Bicarbonate. In acidosis, the excess of acids combines with the alkali, forming a neutral salt, and much larger doses have therefore to be given. The reaction of the urine is tested with litmus paper 1 hour after successive 5 Gm. doses of Sodium Bicarbonate, the urine being first boiled and cooled. The amount of alkali required to render the urine alkaline gives an indication of the degree of acidosis, 30 to 60 Gm. being necessary in moderate cases.

Albumin.

The simplest and most accurate test is to boil the top of a column of urine in a test tube, and if a turbidity appears in the part boiled, add a drop of 5—10% Acetic Acid. Phosphates are dissolved but Albumin remains. The delicacy of the test depends on the contrast between the upper and lower region and the urine must be filtered if it is not clear before the test is conducted.

The only substance likely to mislead is Bence-Jones proteose, a variety of protein excreted by patients suffering from multiple myeloma and occasionally by cases of leukæmia and chronic nephritis. Bence-Jones proteose appears when the urine is heated to about 60° C., and disappears on boiling to reappear when the urine cools.

The Salicylsulphonic Acid test has the advantage that it can be performed in the cold. An equal volume of urine is placed in two test tubes and 2 or 3 drops of 25% solution of Salicylsulphonic acid added to one of them. See also p. 363. In the presence of Albumin the liquid in the tube to which Salicylsulphonic acid was added will appear turbid compared with the control.

Albuminuria may occur in healthy individuals, as functional or postural albuminuria. The albuminuria may disappear when the patient is at rest to reappear on taking exercise or even on assuming the erect posture. In pathological conditions albuminuria is nearly always accompanied by tube casts and under these circumstances it points to organic disease of the kidney, or severe irritation or circulatory changes in the kidney.

Renal Function Tests are dealt with antea, pp. 62-64 and postea, 384-387.

The amount of albumin detected at any time does not measure the importance of the albuminuria. A large output naturally implies failure of nutrition, but a small quantity may be of equal danger. Note Sp. Gr. and color.

Albuminuria. Incidence of in 60,000 men examined. Salicyl-sulphonic acid used. It is undoubtedly one of the most reliable and delicate reagents—six drops of saturated solution to about $\frac{1}{2}$ inch of urine in an ordinary test-tube. Total with gross albuminuria after allowing for pus, etc., about 5%.—H. Maclean, B.M.J. i./19,94.

Egg Albumen in simulated Albuminuria, methods of detection.—Y.B.P. 1919, 57, 59.

Albumin Detection, by heating upper parts of tubes in steam bath.—G. Bousfield, L. i./20,97.

Influenza as an ætiological factor in nephritis.—W. W. D. Thomson and H. F. Macaulay, L. i./20,481.

Cystoscopy, ureteral catheterization and pyelography reliable in determining presence or absence of disease of the kidney.—C. Morson and H. P. Winsbury White, B.M.J. i./22,257.

Pure Albumin free from Globulin can be isolated from the urine by repeated precipitation with Sodium Sulphate. In cases of "albuminuria of pregnancy" (and proteinuria not associated with pregnancy) the Albumin had a specific rotation averaging -55.81° , whereas in eclampsia there were two groups averaging -56.37° and -38.5° . Accordingly, it is suggested that in certain types of eclampsia the urinary Albumin may be mainly *Lactalbumin*, and that eclampsia may be an anaphylactic reaction due to the circulation in the blood of this foreign protein, in which the mammary gland may be an important factor.—A. Hynd, L. ii./25,911,925.

The mere presence of Albumin in the urine of adolescents need not be regarded so gravely as was once the case, provided there are no other signs of renal or constitutional disability. One in every 20 male adolescents exhibits the condition, which may persist throughout life without detriment to physical efficiency. The after-rest specimen is usually free from Albumin. The condition is not associated with any particular type of youth or man.—H. H. Bashford, L. ii./26,1305-7.

The following chemicals are used for albumin detection.—

Asaprol (Calcium Beta-naphthol-Sulphonate) precipitates albumin, peptone, etc., from acid solution. On boiling, peptone and albumose redissolve, albumin remains.

Carbolic Acid (saturated solution in absolute alcohol) has been used as an albumin test, but is not so delicate as Salicyl-sulphonic Acid, but the latter (see below) may be too delicate for clinical work. Further, the milkiness produced by the Phenol emulsifying with the water is a drawback.

Ferrocyanic Acid (Hydroferrocyanic Acid Test).

Potassium Ferrocyanide, $K_4Fe(CN)_6 + 3H_2O$, and Acetic or Citric Acid mixed in solution set free Hydroferrocyanic Acid. Does not precipitate peptones.

The following procedure may be used:—

Solution A.—Citric Acid 10 Gm.; Water 100 Cc.

Solution B.—Potassium Ferrocyanide 10 Gm.; Water 100 Cc.

Add 3 Cc. of Solution A to 4 Cc. of the specimen. Mix and add 3 Cc. of Solution B. In the presence of 0.3% or more of Albumin an immediate pp. is formed. 0.1% is detected on standing one hour. May also be applied as a ring test.

One Cc. of a 10% solution of Acetic Acid and Potassium Ferrocyanide gives a just perceptible clouding when added to urine containing 0.1% albumin.

luted 1 in 100 with water. If the clouding appears with a dilution of 1 in 200 the urine contains 0.2% and so on.—B.M.J.E. ii./27,78.

Meta-Phosphoric Acid, HPO_3 .—A fresh solution of a little of this acid is added to the clear filtered urine. A cloud or precipitation indicates presence of albumin.

Millon's Reagent.—Nitroso-Nitrate of Mercury.—Dissolve Mercury 1 Cc. in Fuming Nitric Acid 27 Cc. without heat and dilute the resulting solution with an equal volume of Distilled Water. With albumin or urea this gives a yellow, then red colouration on heating.

The directions given above are those of the *B.P.* '14. Many modifications of Millon's Reagent have been proposed. The following, for example, is one third of the strength of the *B.P.* '14 solution in Mercury and is possibly the original formula. Dissolve Mercury 1 by weight in Nitric Acid 2 by weight and then dilute with 2 volumes of water.

Nitric Acid Test (Heller's).

Nitric Acid is placed in a test tube and the filtered urine, or diluted filtered urine, carefully 'layered' on to it. A white ring at the junction of the liquids indicates presence of albumin; confirm by Heat and Salicyl Sulphonic tests. Not so delicate as the heat and acetic acid, but will show 1 in 12,000 at once. Bilious urines may produce play of colours characteristic of Gmelin's test.

The test may also be applied by heat—i.e. add a little Nitric Acid, mix and boil the upper portion.

Picric Acid Solution.

Picric Acid 10 Gm., Citric Acid 20 Gm., dissolve in about 900 Cc. boiling water, cool and add water to 1,000 Cc. This reagent is used for the approximate determination of albumin by an Albuminometer which is about six inches long and 0.6 inch in diameter; the graduations on it are the results of experiment and indicate approximately 0.1 up to 0.7% albumin.

By comparison with a standard dried albumin solution, 1 in 1,000 and by heating both to 180° F. and centrifugalising, the process can be terminated in a few minutes.

Mann warns against the voluminous precipitate which one occasionally gets with Esbach's reagent giving a fictitious estimation. Many albuminous urines give a pale blue with the Biuret reaction without any tendency to violet; others will give a reddish purple. Such urine indicates by the reddish color some hydrolytic change and will give the incorrect reading referred to.

For exact determinations, albumin should be precipitated by some suitable reagent, itself nitrogen-free, e.g., carbolic acid or tannin and the washed precipitate, dried and weighed, or better, the nitrogen contained in it should be estimated by a Kjeldahl analysis, the amount of nitrogen found being multiplied by the factor 6.3 to obtain the amount of proteins.

N.B.—Methylene blue precipitates picric acid solution in case of patients undergoing treatment with this compound.

The administration of alkaloids may cause urine to give a precipitate with picric acid, but this is redissolved on heating to the boiling point.

Roberts' Albumin Test.—Nitric Acid 1 part, Solution of Magnesium Sulphate (10 in 13) 4 parts. Is found to be very satisfactory—advantage, high density. Slope the tube containing a little test solution and allow the urine to slowly run down into it with a dropper. Ammonium Nitrate may be used instead of Magnesium Sulphate.

Salicyl-sulphonic Acid.

$\text{C}_6\text{H}_3\text{SO}_3\text{H.OH.COOH} = 218.107.$

In colourless crystals, prepared by action of sulphuric anhydride on salicylic acid. Soluble in water and alcohol. The test is conducted as mentioned, p. 361, or proceed by careful 'layering' of the filtered urine upon a crystal.

An extremely precise, reliable, and quick test, giving a dense white precipitate.

In confirmation note the following:—

Albumin, globulin, myosin, etc., coagulate on heating.

Albumoses dissolve on heating, and reappear on cooling.

Not affected by phosphates, bile, urates or alkaloids.

Pure Peptone is not precipitated, only the intermediate products between Albumin and Peptone in solutions saturated with ammonium sulphate.

***Endolytic Tubes (Albumin).**—Sealed Capillary tubes partially filled with a solution of this Reagent are portable for clinical use. The ends are snapped off and the urine (if necessary, filtered) is drawn into the tube by capillarity. From opalescence to thick precipitate occurs if positive. Distinguish albumose by pouring hot water over the tube—precipitate dissolves as above detailed. *Acetone, Diacetic Acid and Glucose Endolytic Tubes* are also made.

Trichloroacetic Acid. See Vol. I., p. 25. A saturated solution, or a crystal, is used in the same manner as the last test.

May precipitate uric acid and nucleo-proteins.

H. Leslie Roberts communicated a biochemical study of the **Chloroacetic Acids** (Brit. Jl. Dermat. and Syphil., Aug.—Sept., 1926, pp. 323-334, and Oct. 1926, pp. 375-391). The Trichloro substitution product was described by Prof. Heidenhain, for histology, in 1905, as a good tissue-fixing material. It penetrates even large masses of tissue and is useful for demonstrating the structure of epithelial organs. Roberts found it clinically of great value for rodent ulcer and benign epitheliomata (see Vol. I., p. 25), and this bio-chemical research shows that it possesses both hydrophilic and oleophilic properties and dissolves lipoids. Experiments on carbohydrates and parenchyme of fruits are detailed, and the reactions of normal and pathological skin in a variety of affections. The therapeutic effect in rodent ulcer and other epithelial growths is distinguished by solidification of the cell contents, with inhibition of leucocytes and water transudation.

Tannin-Hydrochloric Acid Test.

Mix 5 Cc. of the specimen with 5 Cc. of 1·5% Alcoholic Tannin Solution warm, and add 5 Cc. of Dilute Hydrochloric Acid (1 in 3). Turbidity or yellowish precipitate. Interfering substances such as urates, phosphates and alkaloids are kept in solution by the acid and resins and alkaloids are redissolved by the alcohol and peptones by heating.

Albumoses.

One may safely regard all proteins in urine as albumoses, which dissolve on heating (after precipitation by a reagent, e.g., salicyl-sulphonic acid) and reappear on cooling.

Biuret Reaction.—Albumin, if present, is removed by 10% Trichloroacetic Acid Solution, and the filtrate tested with the **Biuret Test**:—

In a test tube place 1 drop of Copper Sulphate Solution (2%), add 5 Cc. urine, then 5 Cc. of Sodium Hydroxide Solution (10%). A rose pink indicates the presence of albumose.

Nickel Reagent.—2 Cc. solution of 5% Nickel Sulphate with Strong Ammonia is added to 4-5 Cc. of urine made strongly alkaline with Potassium Hydroxide. Protein present gives a white or greenish-white ring while an orange yellow ring is given in the presence of *Albumoses and Peptones*.—J.C.S., A., 11, 1921, 419.

Albumose, Bence-Jones's occurs in myelopathic albumosuria, a disease associated with morbid conditions of the bones. This albumose is detected by (1) coagulating at 58° C. i.e., lower than serum albumin, which coagulates at 75° C., (2) precipitation with *hydrochloric acid*, (3) nitric acid in the cold—on raising to the boiling point, however, the coagulum dissolves more or less completely and reappears on cooling, (4) with potassium ferrocyanide and citric acid (often takes time to develop, differing in

this respect from albumin). The hydrochloric acid test is exceedingly sensitive and does not depend on excess of salts. The result is obtainable after very free dilution of the specimen.—Ref., L.i./13,522.

Amino-Acids.

Tyrosin, Syn. PARA-HYDROXYPHENYL-ALANINE.

$C_6H_4.OH.C_2H_3(NH_2).COOH = 181.096$.

Is recognised by its characteristic crystalline appearance being in shining needles, either in bundles or star form.

Russula delicata.—The juice of this fungus is a test for Tyrosin; changes it from red to black. The fungus has a stem 1 to 2 ins. high, $\frac{1}{2}$ in. or more thick, even, smooth, white cap, fleshy, 3 to 5 ins. broad, funnel-shaped when full grown, regular, even, smooth, margin involute, without striae, flesh firm, dry, white.

Further Tests for Tyrosin :—

Two Cc. of Sulphuric Acid mixed with 3 to 5 drops of a Solution of Aldehyde in twice its volume of Alcohol 90%, care being taken that the liquid remains colourless—a few drops added to the suspected liquid produces a gooseberry red colour. This test is supposed to detect Tyrosin up to 1 in 10,000

Piria states on adding a few drops of strong Sulphuric Acid to a little Tyrosin in a dish it dissolves with slight reddening, on saturating with Barium Carbonate (after diluting) and adding to the filtrate neutral Ferric Chloride Solution a violet colour is formed.—Schmidt.

Ammonium-Sulpho-Molybdate q.v., gives blue to violet colour.

Leucin. α -AMIDO ISO-CAPROIC ACID.

$\begin{matrix} CH_2 \\ CH_2 \end{matrix} > CH-CH_2-CH(NH_2)-CO.OH = 131.112$.

Leucin occurs as an early result of protein cleavage. There are two isomeric forms of it—respectively *laevo*- and *dextro*-.

Is in crystalline spheroidal clumps. An arterial depressor. Has been given in arteriosclerosis.

Histidin $C_6H_7N_3O_2$ is one of a series of bases termed protamines. They occur in the spermatozoa of fish. They give the Biuret reaction. Histidin is frequently found as a decomposition product of Albuminoid bodies. Pyman has synthesised it.—P.J. i./16,108.

Bile and its derivatives.

(With some notes on other abnormal constituents.)

Urobilin and Urobilinogen are best shown by Ehrlich's Aldehyde Reaction, i.e., the UROBILINOGEN TEST (P.G. VI.): Dimethyl-paraminobenzaldehyde, $C_6H_4N(CH_3)_2.CO.H$ (1:4), M.pt. 73° C. Two Gm. dissolved in 98 Cc. of a mixture of Hydrochloric Acid 4 vols. and Water 1 vol.

To 5 Cc. of urine add 2 drops of the solution. A deep red colour is positive. It may be necessary to warm the tube and it often takes a few minutes for the colour to appear.

It will be seen that the parent substances of Indican, viz., Indol C_8H_7N and Indoxyl $C_8H_5(NH)OH$ bear relation chemically with the bodies contained in Urobilinogen, viz., Bilirubin $C_{32}H_{36}N_4O_6$, Hydrobilirubin $C_{32}H_{40}N_4O_7$, etc.

The Urobilinogen Test for liver function advocated for use as a routine laboratory measure in all urine examinations.—Jl.A.M.A. ii./25,1062.

Bile pigments are simply demonstrated by Gmelin's Test. Urine is 'layered' over the surface of strong fuming Nitric Acid in a test tube. With normal urine a purple or yellow colour may appear, but in the presence of bile pigment a green colour develops at the junction of the fluids.

Tincture of Iodine.—A few drops 'layered' on to the specimen and the tube shaken gently, produce a green colour if bile pigment be present.

Chromic Acid. 5% solution added gradually produces a green colour.

The following is a modification :—

To 10 Cc. urine add 2 Cc. of 0.5% solution of Albumin and a few drops of 10% Acetic Acid, boil and filter. The precipitate is washed with water and to it on filter add 1 drop of mixture of 4 Cc. 6% Potassium Dichromate and 1cc. 20% Sulphuric Acid. If bile pigments present the yellow precipitate turns green or bluish-green. This sensitive reaction is not given by other normal or abnormal urinary pigments.—J.C.S., A. ii./1922, 671.

Soulam Nitrite with Sulphuric Acid (Vitali's Reaction) gives green colour.

Ferric Chloride test for bile pigments.

Obermayer Reagent prepared by dissolving 0.3 Gm. Ferric Chloride in 100 Cc. concentrated HCl. 0.5 Cc. of the reagent is added to 5 Cc. of urine, and if bile pigment is present the colour at once appears as deep green—bile may be tested in the same way. For serum, 4 Cc. 95% Alcohol is added to 2 Cc. serum and centrifuged, the supernatant liquor withdrawn and 0.5 Cc. of reagent added—a green colour will appear in a few seconds.—Pres., Aug. '24, 300

Urobilin in malarial patients—conclusions reached from examination of 20 cases of malaria for Urobilin.—B.M.J.E. ii./24, 17.

Bile Salts are shown by Hay's Test. Flowers of Sulphur are sprinkled on the surface of cold urine in a beaker. The powder floats on the surface of normal urine. Bile salts lower surface tension and permit the powdered Sulphur to sink.

Peptone Test.—Peptone, in powder 30, Salicylic Acid 4, Acetic Acid 30, Distilled Water 3,500.

Dissolve and filter. Add one vol. of urine containing bile salts to three vols. of this solution opalescence (or p.p.) appears; it dissolves completely on adding acetic or citric acid, and diminishes, but does not disappear on boiling.—*Oliver*.

Pettenkofer's Test for Bile Salts. Add a few drops of Syrup, shake, and then Sulphuric Acid.—Reddish-violet colour. *cf.* **Acid Cholic** and **Sodii Taurocholas** in **Scheme for recognition of Organic Substances**.

Significance.

The presence of either **urobilin**, **bile pigments** or **bile salts**, indicates some derangement in hepatic functions. Urobilin is found in small quantities in normal urine, but insufficient to be detected by the ordinary tests. It is formed from urobilinogen a decomposition product of bilirubin formed by the action of the intestinal bacteria on the bile which passes into the intestine. Under normal conditions a portion of this is absorbed from the intestine and carried to the liver in the portal blood and there reconverted into bilirubin. When the liver functions are deranged this transformation into bilirubin may be interfered with and urobilinogen reaches the general circulation and is excreted by the kidneys. Thus tests for urobilin may be positive in the preicteric stage of jaundice. Urobilin is increased as the result of excessive blood destruction and in damage to the liver parenchyma. It is nearly or completely absent in obstructive jaundice.

Bile pigments and bile salts usually occur together, although the bile pigment may occur alone. It is seldom necessary, therefore to test for bile salts. The significance of bile in the urine is similar to that of bile staining of the tissues, and is attributable either to obstruction to the outflow of bile from the liver or to excessive destruction of red blood corpuscles. Small amounts of bile may, however, be found in the urine when the disturbance is not severe enough to produce recognisable jaundice, or in other cases, before the jaundice supervenes.

Hæmatoporphyrin (*cf.* Vol. I., p. 795).

Urine of patients taking Trional, Tetronal and Sulphonal should be watched for possible hæmatoporphyrinuria. An account of a case exhibiting.—*L. ii.* / 12,960.

Calculi.

Urinary Calculi.—The size and shape of urinary calculi depend on the region of the urinary tract in which they form. Their chemical composition depends on the character of the urine in which they form. Since the urine may frequently change its character during the slow growth of the stone the end result is usually a laminated calculus with layers of different colour, consistence and chemical composition. There may or may not be an organic nucleus to the calculus. Changes in the reaction of the urine are primarily responsible for the progressive growth of the calculus, increasing acidity causing uric acid to deposit and increasing alkalinity causing deposition of phosphates and urates. It is probable that many calculi centre round a primary uric acid infarct of the tubules of the kidney. The chief secondary changes produced by a calculus are hæmorrhage, infection and the deposition of organic elements round the stone. The commonest varieties of urinary calculi are the calcium oxalate, uric acid, ammonium urate and phosphatic calculi.

Calcium Oxalate stones are extremely hard, usually round and distinguished by their dark brown colour and by their rough 'mulberry' like exterior. They are often formed around a nucleus of uric acid or urates. The irritation caused by the rough surface leads to the deposition of carbonates and phosphates which may fill up the depressions and smooth off the surfaces.

Phosphatic calculi have a rough white crumbly surface. They form when the bladder is inflamed and consist chiefly of ammonio-magnesium phosphate and calcium phosphates and carbonates.

Uric Acid Calculi are smooth and hard, like pebbles. The centre may contain a granule of ammonium urate round which fine delicate yellow laminæ are regularly laid down. A pure uric acid calculus may not show by X-Rays because its permeability is practically the same as surrounding soft tissues but mixed calculi composed of uric acid with Calcium Phosphate or Oxalate may be recognised radiologically.

Other constituents of urinary calculi are Sodium Urate, Xanthin, and Cystin.

Chemical Examination of Urinary Calculi (*Panton and Marrack*).

If the stone is of considerable size cut it in half. If the nucleus differs in appearance from the cortical portion, scrape it out and examine it separately. Powder the calculus and apply the following tests :

(1) Effervescence with dilute Hydrochloric Acid shows Carbonates. May be done microscopically between a slide and cover glass. Carbonates are rarely obtained except as traces.

(2) Incinerate a little powder on platinum foil over a Bunsen flame and add dilute Hydrochloric Acid. If effervescence occurs Oxalates were originally present. If Oxalates or Carbonates are present the base is usually Calcium.

(3) To a pinch of the powder add 2 drops of strong Nitric Acid and evaporate to dryness over a water-bath. If Uric Acid is present a red colour appears which turns reddish violet (Murexide reaction) on adding dilute Ammonia (5 drops of strong solution to about a test-tube full of water). In preference let the dish be covered with another previously moistened with Ammonia.

(4) To test for Ammonium Urate add Caustic Soda and heat—ammoniacal odour. If no Ammonia is evolved and the powder gave the Murexide reaction the material is Uric Acid.

(5) **Phosphates**—Dissolve in dilute warm Hydrochloric Acid, filter and add a few drops of Nitric Acid. Add Ammonium Molybdate solution and warm : a yellow precipitate forms. The phosphates may be earthy or less frequently Ammonio-Magnesium Phosphate. To distinguish between the phosphates test for the presence of Ammonia as in (4).

If any of the above are positive it is not necessary to proceed further, but if negative or only traces of the above are found the following rare constituents may be sought for :—

Cystin.—Burn the powder on platinum foil over the flame. Cystin burns rapidly with a blue flame and gives off a sharp odour. Boil a pinch of the powder with 10% caustic soda and two drops of lead acetate solution. If cystine is present a black precipitate forms.

Dissolve some powder in ammonia. Cystine is readily soluble and on spontaneous evaporation of the ammonia the typical hexagonal plates separate.

Xanthin.—The powder on the platinum foil burns away but without a flame. Try the murexide test. There is no effervescence on adding nitric acid and the residue left after heating is yellow. Add a drop of caustic soda to the dried residue after cooling: in the presence of Xanthin the residue becomes yellow. Warm and the colour changes to red.

Fibrin.—The powder burns on the platinum foil with a yellow flame and an odour of burnt feathers. The powder is insoluble in alcohol or ether, but soluble in hot caustic potash. Add Acetic Acid to the hot caustic potash solution. The fibrin is precipitated with an evolution of H_2S .

Urostealith.—The powder burns with a yellow flame and an odour of resin. It is soluble in alcohol and ether.

Further data in Edn. XVIII., Vol. II., p. 403.

Biliary Calculi (Gall Stones). Concretions forming in the gall bladder and bile ducts.

Cholesterol content of the blood an important agent in causation.—In uncomplicated cases of cholelithiasis the content tends to be high. In such the blood value ranged from 0.133 to 0.409%. The average normal is 0.16%.—Sir Berkeley Moynihan, L. ii./23,4. See also J. Sherren, *ibid.* 7.

Cholesterol content of blood serum after irradiation with X-Rays.—B.C.A. '28, A1152.

Cast.

The presence of casts may be an important indication of renal disease. The centrifuged deposit is examined both with the 2/3 and later with the 1/6 inch objective. Casts have a sharp outline. Their significance depends on their character.

Cellular casts may be composed of red blood corpuscles, pus cells or the mononuclear cells of renal epithelium, and indicate acute nephritis. In chronic parenchymatous nephritis and in acute nephritis after the first few days of the disease the casts are usually granular, and represent a later stage of the cellular casts which have undergone a granular degeneration.

Hyaline casts, with structureless contents, may be found in any form of nephritis but are commonest in chronic interstitial nephritis and hyperpiesia. A few hyaline casts may be present in the urine of healthy people.

Cylindroids are pale ribbon-like bodies with tapering ends which are found in inflammations of the urinary tract.

Chlorides.

Instead of evaporating and incinerating with ammonium nitrate, oxidise the organic matter contained in 10 to 20 Cc. urine by warming with 3 Cc. of Sulphuric Acid and a slight excess of Potassium Permanganate solution. The addition of a few drops of Hydrogen Peroxide will then cause the precipitated Manganese Dioxide to dissolve giving a clear solution. To this add a few Cc. of Nitric Acid and a measured excess of N/10 Silver Nitrate solution, boil and cool. After adding 1 or 2 Cc. of Ferric Alum solution to the mixture, titrate the excess of Silver with N/10 Ammonium Thiocyanate.

Creatinine.

Glycocoll-Methyl-Guanidin. $C_4H_7N_3O = 113.08$

To test for this body in the Urine add a little Sodium Nitro-Prusside and Caustic Soda. A red colour develops which fades on boiling the mixture. If a little Acetic Acid be added to the boiling liquid, Prussian Blue is produced.

Creatinine, Creatine and Mucin have retarding effect on the precipitation of Cuprous Oxide from Fehling's Solution. Urates have auxiliary effect.

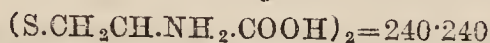
Excretion of Creatinine in diabetes mellitus.—There appears to be some connection between carbohydrate metabolism and the Creatine-creatinine metabolism. Experiments with diabetic urines showed that Creatinine was not

increased to any extent even when patients were on a highly nitrogenous diet. Creatine on the other hand, a substance never found in the normal urine if the diet be free from Creatine and Creatinine was always found—even when patient was on a Creatine-Creatinine-free diet.—B.M.J. ii./10, 1343.

Creatinine and Creatine in Blood. Method of estimation by means of the Hellige Colorimeter.—See 'Blood and Urine Chemistry.'—Gradwohl and Blaivas, 1920.

Kidney Permeability. Creatinine as Test, see p. 64.

Cystin.



Cystin is a cleavage product of protein-metabolism, apparently loosely bound and easily split off at an early period of the intestinal digestion. Normally it becomes oxidised and hence is unrecognisable, but in cystinuria it is excreted unchanged.

Separation of Cystin. Free from oxalates and phosphates by Ammonia and subsequent addition of Calcium Chloride until this no longer precipitates, add equal volume of Acetone and Acetic Acid in slight excess. Cystin crystallises out in 3 or 4 days, and may be purified by dissolving in Ammonia and reprecipitating.—Mann.

Is occasionally found in urinary deposits as transparent six-sided crystals—insoluble in alcohol but soluble with ease in mineral acids, caustic alkalis and ammonia. Uric acid occasionally crystallises in similar form, but gives the murexide reaction; Cystin does not.

Dextrin.

Twenty Cc. of the filtered urine is placed in a small flask, and 2 Cc. of hydrochloric acid (Sp. Gr. 1·16) added. The neck of the flask is closed with a small funnel and the contents are gently boiled for ten minutes. The excess of hydrochloric acid is then neutralised by adding 5 Cc. of a saturated solution of sodium carbonate, and the flask is cooled under running water. After making the contents faintly acid with acetic acid and shaking until frothing ceases, they are poured into a 50 Cc. graduated flask and the transference completed with two or three small washings of water. The contents are now well shaken with 5 Gm. of tribasic lead acetate, made up to 50 Cc. with water, allowed to stand ten minutes, and filtered, repeating if necessary until a clear filtrate (A) is obtained. In another flask 20 Cc. of the original urine is shaken with 5 Gm. of tribasic lead acetate, made up to 50 Cc. with water, and filtered, yielding a second clear filtrate (B). Into each of two small flasks is now introduced 10 Cc. of a specially prepared copper solution, and to one is added 5 Cc. of the filtrate "A" and to the other 5 Cc. of the filtrate "B." The necks of the flasks are closed with small funnels and the flasks are heated in a boiling saturated solution of sodium chloride for exactly five minutes. The flasks are then cooled in running water and 3 Cc. of sulphuric acid (30%) is added to each from a pipette, after which the contents are titrated with freshly made N/100 sodium thiosulphate solution, using three drops of 1% starch solution as an indicator. The figure obtained by titrating a control, consisting of 10 Cc. of the special copper solution and 3 Cc. of sulphuric acid (30%), with the same dilution of thiosulphate and starch as the indicator, is subtracted from each of the findings. The difference between the results thus obtained, multiplied by 5,000 and divided by 6, gives, approximately, the dextrin value of the urine in milligrams per cent. The special copper solution is prepared as follows:—
I. Copper sulphate 5 Gm., tartaric acid 7·5 Gm., potassium carbonate 59 Gm., distilled water 400 Cc. II. Potassium iodide 10 Gm., potassium biniodate 0·7 Gm., potassium oxalate 13·4 Gm., distilled water 250 Cc. Mix and make up to 1,000 Cc. This method does not give reliable results in the presence of lævulose, lactose, or maltose, and should not be used when there is more than 0·1% of dextrose. It is then necessary to employ the author's modification of Jolles's process for estimating pentose. By either method an excretion of dextrin exceeding 150 mg. for twenty-four hours may be considered as abnormal.—A Revision of a previous test.—P. J. Cammidge, L. ii./27, 1388.

Formaldehyde.

We had occasion to conduct some examinations of Urine for formaldehyde to determine whether excretion of Formaldehyde occurs after administration of Hexamine and allied bodies (*cf.* Hexamine Vol. I., and this vol.). We found the following tests of service :—

Phloroglucin Test.

To 5 or 10 Cc. of sample add 5 drops of 1% Aqueous Solution of Phloroglucin followed by 5 drops of 30% Caustic Soda Solution. Red color appears if formaldehyde present.

Will show 1 in 2,000,000 of Water and 1 in 50,000 of urine.

(Shows no color with Hexamine.)

Rimini's Test.

To 5 or 6 Cc. of sample add 1 drop of 1% Aqueous Solution of Phenylhydrazine, then 1 drop of 1% Aqueous Solution of Sodium Nitroprusside and 5 drops of 30% Caustic Soda Solution.

Blue color appears if Formaldehyde be present.

Will show 1 in 75,000 of water and 1 in 100,000 of urine.

(Shows no color with Hexamine.)

1 in 150,000 of urine can be seen

'Meta' Test (W. H. M.).

To 10 Cc. of sample add 0.05 Cc. of 5% Aqueous Solution of Meta-diamidobenzol Hydrochloride.

Gives a yellow color or precipitate if Formaldehyde present.

Will show 1 in 20,000 of water by color and 1 or 2 in 10,000 of urine by opalescence or precipitate.

(Gives no reaction with Hexamine.)

The 'Meta' Test in conjunction with the others may prove of value in searching for Formaldehyde in milk or food.

Glucose.

Sp. Gr. of Diabetic Urines.

The comparison of the sugar content of 200 specimens of glycosuric urines, examined in our laboratories, with their Specific Gravities, gave the following interesting figures.

SUGAR. CONTENT.	MINI- MUM CON- TENT.	MAXI- MUM CON- TENT.	MINI- MUM SP. GR.	MAXI- MUM SP. GR.	AVERAGE CONTENT.	AVER- AGE SP. GR.
1% or less	0.25%	1%	1.004	1.035	0.684%	1.0184
1—2%	1.05%	1.9%	1.008	1.035	1.329%	1.0226
2—3%	2.00%	2.9%	1.010	1.036	2.461%	1.0274
3—4%	3.10%	3.7%	1.020	1.040	3.418%	1.0305
4—5%	4.00%	4.8%	1.022	1.040	4.347%	1.0316
5—6%	5.00%	5.9%	1.022	1.040	5.360%	1.0330
6% or more	6.30%	9.1%	1.030	1.045	6.956%	1.0371

It is shown that whilst on an average there is a steady increase in the Sp. Gr. comparable with the amount of Glucose present, yet a urine containing 6% or more of sugar may have a lower Sp. Gr. than one in which there is less than 1% sugar.

Benedict's Tests for sugar in urine are popular at the present time. They are simpler and avoid the fallacies of Fehling's Test. Personally, we favour **Gerrard's Solution** in quantitative work, having used it for years with good results.

Benedict's (Quantitative) Modified Fehling Test.

Copper Sulphate 18 Gm., Sodium Carbonate Cryst. 200 Gm., Sodium Citrate 200 Gm., Potassium Sulphocyanide 125 Gm., 5% Potassium Ferrocyanide Solution 5 Cc., Water to 1 litre. The test is as Fehling's—the end point being disappearance of the blue colour.

To conduct the test 25 Cc. of the reagent are measured into a small flask and about 4 Gm. anhydrous Sodium Carbonate added and the solution brought to the boil. Urine is then run in slowly from a burette until the reagent turns from clear blue to an opalescent bluish-white colour when the additions are made more carefully until the colour disappears. This gives a rough indication of the amount of sugar in the urine and the titration is repeated after first diluting the urine so that about 10 Cc. will reduce the reagent. 25 Cc. of the reagent are reduced by 0.05 Gm. Glucose. This quantity is therefore in the volume of urine reducing 25 Cc. of the reagent.

Benedict's Qualitative Test.

Dissolve with heat Sodium (or Potassium) Citrate 173 Gm. and 100 Gm. of anhydrous (or 200 Gm. cryst.) Sodium Carbonate in water, about 700 Cc. Dissolve separately pure crystallised Copper Sulphate 17.3 Gm. in water about 100 Cc. Cool to room temperature, pour the second into the first solution slowly with stirring and make up to 1,000 Cc. with diluted water.

The patient can employ the test himself. 5 Cc. are boiled with 8 drops of urine for two minutes and cooled. If Glucose is present the colour changes to an opalescent green, or in the case of a large quantity of sugar to an opaque red. Benedict's Reagent is reduced by Glucose, Lævulose, Lactose, Pentose and Homogentisic Acid, but not by Uric Acid and Creatinine: hence a positive Benedict's Test indicates some derangement of carbohydrate metabolism (Dodds).

To confirm and distinguish Glucose employ the Fermentation Test, q.v.

If more than 0.5% glucose is present, a precipitate forms after about 30 seconds from onset of boiling, which should be continued for 2 mins. If the solution remains blue, less than 0.1% of sugar is present, but if it turns green there is more than that amount.—G. Graham, L. ii./23, 663.

In cases of pronounced uricæmia, the treated urine develops a turbidity of the colour of Turnbull's Blue, after about 12 hours—the reagent thus also detecting Uric Acid.—J.C.S., A. ii./23, 587. (A slightly modified formula for the reagent is given here.)

Cambridge's Modified Benedict (Qualitative) Test for Quantitative Estimation. (Distinguish from both the foregoing.)

Dissolve by aid of heat Sodium Citrate and Crystallised Sodium Carbonate of each 200 Gm. and Sodium Bicarbonate 10 Gm. in 600 Cc. of Distilled Water, and add to this with constant stirring a solution of 21 Gm. Crystallised Copper Sulphate in about 150 Cc. of water. When cold make up to 1000 Cc.

A very small proportion of urine gives an unmistakable reaction even with a low percentage of sugar, and it is not appreciably reduced by Uric Acid, Creatinin, etc.

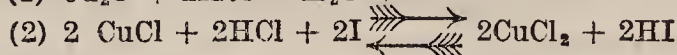
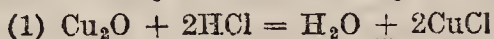
It is employed instead of Fehling's Solution in a modification of Scales' Volumetric Method for estimation of Sugar in urine and blood.—P. J. Cambridge, L. i./17, 613.

Method of procedure:—

The estimation is conducted by boiling a given quantity of the urine with a given quantity of the solution, hydrochloric acid is added to dissolve the cuprous oxide. It also liberates carbon dioxide which protects the cuprous chloride from atmospheric oxidation. The cuprous chloride solution is added to a given quantity in excess, of standard volumetric N/10 Iodine solution and the excess of iodine is titrated with N/20 thiosulphate (the official N/10 will do equally well), using starch as indicator.

Each Cc. of N/10 Iodine Solution = 0.00338 Gm. Glucose.

The reaction may be indicated by the following:—



We tried the process on a 0.5% and a 5% Glucose Solution:

(1) 5 Cc. of 0.5% solution of glucose were boiled for 15 minutes with 20 Cc. of the modified Benedict's reagent. Then dilute hydrochloric acid *q.s.* was added to dissolve all the cuprous oxide formed. N/10 iodine solution 20 Cc. were added and titrated back with N/10 Sodium Thiosulphate using starch as indicator. 12.9 Cc. of the latter were required, *i.e.*, volume of N/10 iodine decolorised = 7.1 Cc., therefore 5 Cc. of the 0.5% glucose solution contain (0.00338×7.1) Gm. = 0.023998 Gm., *i.e.* 0.47996% glucose. On repeating, 0.49354% glucose was found.

(2) Operating on a 5% solution 1 Cc. was boiled for 15 minutes with 40 Cc. of the reagent, hydrochloric acid added and 20 Cc. N/10 iodine. For back titration 5.5 Cc. N/10 thiosulphate were required, *i.e.* 14.5 Cc. N/10 iodine were decolorised, *i.e.* 1 Cc. of the solution under test contains 0.04901 Gm. glucose or 4.901% glucose.

We found there is considerable difficulty in determining the end point in the titration with Thiosulphate, as the weak solution of cupric chloride formed is also a blue colour.

As a rule sugar does not appear in the urine until the percentage in the blood reaches 0.18%. By blood examinations diabetes can therefore be diagnosed with ease at a much earlier stage than when reliance is placed solely on the results of analysis of the urine.

The Allen fasting treatment of the disease is dealt with. The only drug giving any decided benefit is Belladonna and the alkaloid Atropine.—P. J. Cammidge, Pres., Oct. '20.

Estimation of Glucose with Benedict's Reagent.—F. Wokes, P.J. II./24, 117,169. See also E. C. Doss L.ii./28,1200.

Significance of Glycosuria.

The absorption, circulation and utilisation of sugar depend on the harmonious activity of many different organs of the body and glycosuria may result from the breakdown of this cooperative activity at different points. It is most important to remember that glycosuria does not necessarily indicate diabetes. It is only after the exclusion of the less serious causes of glycosuria that a diagnosis of diabetes is justified. All carbohydrate is absorbed from the intestine in the form of the monosaccharide, glucose, to be taken to the liver *via* the portal vein and there stored as glycogen. Just enough carbohydrate is delivered by the liver to the blood to keep the circulating blood-sugar constant at a level of about 100 mgr. per 100 Cc. The blood glucose is used up by the tissues which oxidise it to CO_2 and water. Normally the kidney will only excrete sugar from the blood when the blood sugar rises above 180 mgr. per 100 Cc. (leak point of kidney).

Alimentary Glycosuria results when sugar is absorbed from the intestine quicker than it can be stored in the liver, so that the blood sugar rises and the leak point is passed. This is not a

common occurrence, and experiments have shown that it is difficult to produce alimentary glycosuria in healthy individuals even after the consumption of enormous quantities of sugar.

Renal Glycosuria results when the leak point of the kidney is set at a lower figure than normal. Thus some individuals excrete sugar in the urine even when the blood sugar is only 140 mgr. per 100 Cc. In such people glycosuria appears after a carbohydrate meal when the blood sugar is likely to rise. Renal glycosuria is an innocent condition, but it is advisable to keep such patients under observation.

Endocrine Glycosuria occurs in hyperthyroidism, pituitary tumours and after injections of adrenalin. These hormones probably act by stimulating the liver to break down glycogen, with the result that hyperglycæmia and glycosuria result.

Injuries to the floor of the fourth ventricle cause sugar to appear in the urine, and this has been described as **Nervous Glycosuria**. The probable explanation is that injuries to this region of the brain cause a stimulus to the suprarenals with an increase in the adrenalin in the blood, and therefore an adrenalin glycosuria.

True Diabetes results from the inability of the tissues to utilise carbohydrate, owing to the absence of insulin provided by the pancreas. This inability to utilise carbohydrate is interpreted by the body as a stimulus for the production of more glucose so that all available carbohydrate is poured into the blood, producing a hyperglycæmia. Since the tissues cannot utilise the sugar it is excreted in the urine.

These different forms of glycosuria can be distinguished by estimations of the blood sugar and observation of the glucose tolerance test.

Phloridzin Glycosuria. This was first observed by Mering who by giving 1 Gm. of Phloridzin night and morning, produced the daily excretion of nearly 100 Gm. of glucose in the urine. In phloridzin glycosuria there is no increase of glucose in the blood. According to one hypothesis the phloridzin is split up in the kidneys into sugar, and phloretin. *Vide also* this vol., p. 63, and Vol. I., p. 877.

Further Glucose Reagents.

Fehling's Solution, Potassio-Cupric Tartrate Solution.

Glucose being an aldehyde has strong reducing action. In the test the alkaline glucose-cupric oxide when heated causes deposition of the cuprous oxide. 1 molecule of Glucose reduces practically 5 molecules of Cupric Oxide.

In making use of Fehling's Solution it is important when looking for small quantities of sugar to dilute the urine to about Sp. Gr. 1.015. Mix with an equal volume of mixed Fehling's Solution. Boil for a few seconds—if no precipitate within two minutes there is no sugar of pathological import. For Life Insurance purposes the Alkaline Safranine test (*q.v.*) deserves to come more into use.

Fermentation and other tests should be used in doubtful cases.

Great care, however, should be taken not to confuse with reducing substances other than glucose. Personally we have great faith in Allen's modification of the test, *q.v.*

Fehling's Solution is prepared in two solutions:—No. 1. Copper Sulphate 34·64, Sulphuric Acid 0·5, Distilled Water to 500.

No. 2. Sodium Hydroxide 77, Sodium Potassium Tartrate 176, Distilled Water to 500.

Mix equal volumes when required. Of this, 10 Cc. will be decolourised and reduced by 0·05 Gm. (or 53 minims = $\frac{1}{4}$ grain) of glucose or diabetic sugar in solution, with precipitation of yellowish red cuprous oxide when the two are boiled together. No. 2 solution should not be kept in a very cold place or it may crystallise. By keeping the copper solution separate from the alkaline solution the test is prevented from becoming erroneously sensitive.

A little Calcium Carbonate or Barium Sulphate greatly assists the deposition of the cuprous oxide and enables the colour of the supernatant liquor to be more easily seen.

On p. 376 we give a Table shewing equivalents in glucose when using **Gerrard-Fehling Solution**. The figures there given apply exactly as if 10 Cc. of 'Fehling's' were used in place of the **Gerrard's Solution**.

Sterules, containing 1 Cc. Fehling's Solution, are available.

Glucose * Endolytic Tubes are prepared—use similar to those for Albumin *q.v.*

The reaction may be obtained in the cold or by pouring boiling water on to the charged tube (sealing is not necessary). Or, indeed, if not available a lighted vesta drawn carefully along the tube will suffice. If done in the cold, sealed tube to be inspected for usual cuprous oxide precipitate after 12 to 24 hours.

"Fehling" is reduced by dextrose, levulose, mannitose, milk sugar, galactose, arabinose, aldehyde, formaldehyde (see below), chloral, chloroform, creatinin, valeraldehyde, resorcinol, pyrogallie acid, gallotannic acid, arsenious anhydride, and similar reducing-bodies, glucosides, and acetone, also by

Glycuronic Acid $C_6H_{10}O_7$ = 194·01, Uric Acid. Creatinin, Pyrocatechin, Hydroquinone, Salicylic Acid Compounds; these may be removed by simple repeated **filtration** through **animal Charcoal**. None of these bodies **ferment** or give **Osazone Crystals**. *Vide* Phenylhydrazin Tests.

Glycuronic Acid is closely allied to the Pentoses. It conjugates with **phenol indoxyl** and **skatoxyl**, and normally occurs chiefly as phenol-glycuronic acid in combination with potassium.—Mann.

Tollen's Test for Glycuronates consists in boiling the urine for 1 minute with an equal volume of Conc. Hydrochloric Acid and a small quantity of a solution of Naphtho-resorcin in Alcohol. After cooling and shaking with Ether, the Ether layer will be coloured violet to red if Glycuronates are present.—F. Wokes, P.J. ii./25,127.

Formaldehyde being an Aldehyde, like Glucose *also reduces*,—should not be used to preserve urines for examination as to diabetes. If in doubt as to presence of Formalin for any reason boil with excess of Strong Ammonia Solution before conducting Fehling's test. Another reason for refraining from its use is that Formalin combines with Urea forming crystals on the side of the container not unlike Leucin.

Santonin occasionally prescribed for diabetes, may cause trouble in testing for sugar by production of a red colour with the Fehling's. This may be obviated by adding glacial Acetic Acid to the hot mixture until the blue colour again becomes evident.—P.J. i./25,660.

Phenoquin, **Salicylates**, and **Tolysin** give reducing substances which may be confused with sugar.—per P.J. i./27,362.

Lloyd's 'Reagent' (ALUMINIUM SILICATE; FULLERS' EARTH), removes interfering substances.

To 5 Cc. urine add 5 Cc. N/10 Sulphuric Acid and 10 Cc. water. Add 115 Gm. Lloyd's Alkaloidal Reagent and shake gently for 2 minutes. This removes most of the colouring matters, Uric Acid, Creatin, Creatinin, yet,

unlike Charcoals, does not take away the sugar. (It is not necessary to remove every trace of Creatinin.) Filter. 2 Cc. used for the usual colorimetric sugar determination. Shaking should not be continued for longer than 2 minutes, as acid gradually dissolves the reagent—the dissolved Aluminate does not, however, interfere. With more dilute urines, use 10—15 Cc. For total sugars invert 10 Cc. of above filtrate by heating in boiling water for 75 minutes with 1 Cc. 10% Hydrochloric Acid. Cool, neutralise to Phenolphthalein, dilute to 20 Cc., add a small pinch of Lloyd's reagent, shake, and immediately filter. Take 2 Cc. for determination. Dilute sugar standards found to keep perfectly in 0.3% Benzoic Acid solutions.—Otto Folin and Hilding Berghund, *Jl. Biol. Chem.*, Vol. 51, 1922, 209; Y.B.P. '27, 97.

The Reagent also adsorbs alkaloids in acid solution. These adsorbed alkaloids are liberated and regain their previous solubility in alkaline solutions. Adsorbed alkaloids are practically tasteless, can be introduced into the system, and are liberated only in the digestive tract.—B.C.A., 1913, 2663.

Reducing substances in the urine; their detection and identification.—J. P. Bose, I.M.G., *Apl.* '26, 173.

Uric Acid and Urates in the presence of oxalates and biphosphates reduce Fehling's.—Y.B.P. '27, 94, but Uric Acid does not introduce any great error by its reduction of Fehling's Solution. Our experiments showed that 1% Uric Acid completely reduced an equal volume of Fehling's with about one minute's boiling. There was a slight reduction with a 0.1% solution with Fehling's but none with Nylander's reagent. 10 Cc. Fehling's (=0.05 Gm. of Glucose) by Gerrard's process required 14 Cc. 1% Uric Acid = 0.14 Gram which would be equivalent to 250 Cc. Normal urine approximately which would = 0.02% + error in estimating Glucose, *i.e.*, the amount is negligible. Consequently Uric Acid does not hinder the reduction of Fehling's Solution by glucose.

"Fehling" is not reduced by mannite, dulcite, sucrose, inosite, cellulose, dextrin, arabin, alcohol, glycerin, phenol, benzaldehyde, salicyl aldehyde, acetic, lactic, oxalic, succinic, tartaric, citric, gallic, saccharic, mucic, gluconic, benzoic, salicylic, and sulphurous acids, and alkaloids.

TRICHLORACETIC ACID does not reduce Fehling itself, but tends to inhibit the reduction by sugars, so that *quantitative* results cannot be obtained in its presence.

An orange precipitate formed when hot urine is mixed with hot Fehling's Solution without reboiling, affords almost conclusive evidence of presence of a hexose monosaccharide such as glucose or laevulose.

An orange precipitate formed on boiling is sometimes due to presence of a compound glycuronate. **To make certain of Glucose the urine must contain a + rotatory reducing substance, fermented by yeast** (both Glucose and Laevulose are), it must yield **an Osazone of the correct crystalline form, melting at slightly above 200° C** (both Glucose and Laevulose give) and finally it must yield **no Osazone** in case of Glucose **with Methylphenylhydrazine**, which with Laevulose yields one melting at 150° C.—A. E. Garrod *L. i* 12, 484.

Allen's Modification of Fehling's Test. (*We place great reliance on this test.*—W.H.M.)—For small quantities of sugar in urine. Heat 8 Cc. of the urine to boiling point and add 5 Cc. of the copper solution, cool and add 2 Cc. saturated solution of sodium acetate, slightly acidified with acetic acid, to complete precipitation of uric acid, phosphates, and xanthine. Filter, add 5 Cc. of the alkaline solution, and boil for a few seconds. If more than 0.25 per cent. of sugar be present, cuprous oxide is precipitated before boiling point is reached, but if less than this proportion, it is deposited during cooling.

Gerrard's Solution.

This is prepared by diluting 100 Cc. mixed Fehling Solution with about 300 Cc. of water and almost decolourising, whilst boiling, with 5% solution of Potassium Cyanide (using good commercial cyanide,

about 63 Cc. are required), and making up the volume when cold to 500 Cc.

Method of Use.—Mix 50 Cc. of the solution with 10 Cc. of mixed Fehling's Solution (5 Cc. Fehling's No. 1, and 5 Cc. Fehling's No. 2). Boil in a basin and drop into it, whilst boiling, diluted urine, $\frac{1}{2}$ to 1 Cc. at a time by means of a burette, until the blue colouration just disappears, taking care not to add an excess. An average diabetic urine may be diluted 1 with water to 10.

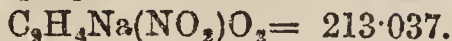
The number of Cc. of actual undiluted urine used contains 0·05 Gm. of Glucose. From this the percentage—grammes per 100 Cc.—is easily obtained. To convert this into grains per fl. oz. multiply by 4·375. The product multiplied by 20 gives the number of grains per pint. The following table will be found useful :—

	No. of Cc. of diluted Urine used.	Gm. Sugar per 100 Cc.	Grains per fl. oz.	Grains per pint.		No. of Cc. of diluted Urine. used.†	Gm. Sugar. per 100 Cc.	Grains per fl. oz.	Grains per pint
Urine diluted 1 with Water to 10	4.0	12.5	54.69	1093.80	Urine diluted 1 with Water to 2	3.0	3.30	14.45	289.00
	4.5	11.1	48.56	971.20		3.5	2.90	12.70	254.00
	5.0	10.0	43.75	875.00		4.0	2.50	10.95	219.00
	5.5	9.1	39.86	797.20		4.5	2.20	9.64	192.80
	6.0	8.3	36.35	727.00		5.0	2.00	8.76	175.20
	6.5	7.7	33.73	674.60		5.5	1.80	7.88	157.60
	7.0	7.1	31.10	622.00		6.0	1.70	7.45	149.00
	7.5	6.7	29.35	587.00		6.5	1.50	6.57	131.40
	8.0	6.3	27.59	551.80		7.0	1.40	6.13	122.60
	8.5	5.9	25.84	517.80		7.5	1.30	5.69	113.80
	9.0	5.6	24.97	499.40		8.0	1.25	5.49	108.80
	9.5	5.3	23.21	464.20		8.5	1.18	5.17	103.40
	10.0	5.0	21.90	438.00		9.0	1.11	4.86	97.40
	10.5	4.8	21.02	420.40		9.5	1.05	4.60	92.00
	11.0	4.5	19.71	394.20		10.0	1.00	4.38	87.60
11.5	4.3	18.83	376.60	10.5	0.95	4.15	83.00		
12.0	4.2	18.40	368.00	11.0	0.91	3.96	79.20		
12.5	4.0	17.52	350.40	11.5	0.87	3.81	76.20		
13.0	3.8	16.61	332.20	12.0	0.83	3.64	72.80		
13.5	3.7	16.21	325.20	12.5	0.80	3.50	70.00		
14.0	3.6	15.77	314.40	13.0	0.77	3.37	67.40		
14.5	3.4	14.86	297.20	13.5	0.74	3.24	64.80		
				14.0	0.71	3.11	62.20		
				14.5	0.69	3.09	61.80		
				15.0	0.67	3.00	60.00		

dextrose solutions on merely heating to boiling while 1% solutions of maltose or lactose do not show reduction under similar conditions.—J.C.S.A. ii./21,525.

Johnson's Test.—See Picric Acid, *postea*.

Nitropropiol. Sodium Orthonitrophenylpropiolate.



Owing to reduction, Indigo blue colour is produced, or indigo-blue itself precipitated. Tablets are prepared. This reaction is based upon Bayer's synthesis of indigo-blue (*q.v.*), which is briefly:—Cinnamic Acid \rightarrow Orthonitrocinnamic Acid \rightarrow Dibromo compound of \rightarrow Orthonitrophenylpropionic Acid, which, warmed with alkali, in the presence of Glucose decomposes thus:— $2\text{C}_9\text{H}_5(\text{NO}_2)\text{O}_2 = \text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2$ (Indigo Blue) + $2\text{CO}_2 + \text{O}_2$. This substance is to be distinguished from Sodium phenyl-propiolate (*Syn. Thermiol*) For testing permeability of the kidney with Indigo-carmin, *v. idem*.

Sodium o-Nitrophenylpropiolate Solution is employed of following composition: Place 5 Gm. of o-nitrophenyl-propionic acid in a mortar and wash alternately with 1 to 2 Cc. of water and 1 to 2 Cc. of 10% Sodium Hydrate Solution until dissolved (altogether about 8 to 10 Cc. required). Dilute to 1 litre. On boiling 5 Cc. with 1 Cc. of Urine blue colour of indigo appears either immediately or in $\frac{1}{2}$ minute according to amount of glucose.

Nylander's Reagent.

Bismuth Subnitrate 2, Rochelle Salt 4, Sodium Hydroxide Solution (8%) 100; and **Almen's** reagent consisting of Bismuth Subnitrate 1, Rochelle Salt 2, Potassium Hydroxide Solution (35% strength) 50, are used for detecting Glucose. The reagents may be reduced by sunlight and hence should be stored in bottles of actinic glass. A small quantity of either warmed with the urine will blacken if glucose be present.

This reagent is not interfered with by the presence of Uric Acid. Even a 1% Solution of the acid we found failed to produce any appreciable reduction on boiling 5 minutes.

Cramer's Mercury Test.—Dissolve Mercuric Oxide (red or yellow) 0.4, with Potassium Iodide 6, in water 100 and adjust alkalinity of the solution so that 10 Cc. are neutralised to phenolphthalein by 2.5 Cc. of N/10 Acid.

To use the test heat 3 Cc. of the soln. to boiling and add 0.3 Cc. of Urine and boil again. On removing from flame the mixture darkens if sugar is present. Metallic Mercury settles ultimately. Glucose, lactose, maltose, xylose and arabinose give the reaction, but not cane sugar.—*Biochem. Jl.*, March 1915, L. i./15,1192.

It is quite sensitive. The deposit of metallic mercury is of greyish colour.

Phenyl-hydrazine Hydrochloride, $\text{C}_6\text{H}_5\text{.NH.NH}_2\text{.HCl} = 144.545$. Is used as a test for sugar. It is in colourless, shining, crystalline scales; and should be free from azo-compounds. A small quantity is warmed with twice its weight of sodium acetate in solution, an equal volume of the suspected solution added, and boiled for 20 minutes. On cooling, yellow crystals of **phenyl-glucosazone**, $\text{C}_{12}\text{H}_{11}\text{O}_4(\text{N.H.C}_6\text{H}_5)_2 = 358.208$ are deposited if sugar be present.—**Osazone Reaction.**

This substance should be handled with care as it may produce eczema.

Boil 2 to 3 Cc. of the urine with equal quantity of water and phenylhydrazine hydrochloride 0.1 Gm. and Sodium Acetate 0.5 Gm. Add 10 Cc. of Sodium Hydrate 10% solution, invert test tube a few times and allow to stand. A pink to red colour of the whole liquid in 5 minutes indicates sugar of clinical significance.

Osazone Reaction in Health. Urines from more than 700 sources showed that 20—30% voided 1 to 2 hours after an ordinary meal yielded typical glucosazone crystals, the percentage dropping to 12—15 in urines passed 4 to 5 hours after meals.—*B.C.A.*, Nov. '28, 1273. For earlier Refs. on this matter see *Edn. XVIII.*, Vol. II., pp. 409, 410.

(**ERYTHREMIA** treated with Phenylhydrazin Hydrochloride. A uniform decrease of hæmoglobin and red blood cells occurred and with three patients with hypertension a reduction in blood pressure. One of the early effects of the drug is a leucocytosis. Initial dose 0.2 Gm. daily for 3 or 4 days and then 0.1 Gm. daily until leucocytes increase in number, or hæmoglobin falls below 100%, when 0.1 Gm. may be given every 2nd or 3rd day, or treatment stopped. Marked rise of leucocytes indicates discontinuance of drug. If

hæmoglobin or red cells begin to rise or leucocytes to fall, dose should be started again or increased in frequency. Usually, 1 Gm. weekly will keep blood count within normal limits. No ill-effects noted, but there is a possibility of danger owing to toxic action of the drug on the liver. This may perhaps be overcome by substituting another of the Hydrazin compounds, e.g., Acetylphenylhydrazin.—Trevor Owen, *Jl. A.M.A.* ii./25, 2027-32. See also Vol. I., p. 1060.)

Picric Acid. JOHNSON'S or BRAUN'S TEST. This has been suggested as a test for Glucose in urine, as a solution of this sugar, if boiled with Picric Acid and Solution of Potash, reduces the yellow Picric Acid to the deep red Picramic Acid. $C_6H_2(NO_2)_3OH + 9H_2 = C_6H_2(NH_2)_3OH + 6H_2O = 139.096$ forming Potassium Picramate the depth of colour depending on the amount of sugar. By the aid of **Johnson's Picro-Saccharometer** this reaction is made quantitative. Solution for use with same: Strong Solution of Ferric Acetate (B.P. '85) 15 drachms, Glacial Acetic Acid $7\frac{1}{2}$ ounces, Ammonia Solution 0.959. $3\frac{3}{4}$ ounces. Water to 3 pints.

Safranine Solution.—1 in 1,000. One volume of this, with one of urine and one of liquor potassæ is heated to boiling, avoiding agitation. If the urine contain sugar to the extent of 0.1% the liquid will be decolourised. (On cooling colour may return in proportion to the amount of sugar present.) Each additional volume of the safranine solution that may be decolourised represents roughly 0.1% of sugar.

Safranine Solution (unlike Fehling's Solution) is unaffected by Creatin, Creatinine, Uric Acid and Urates. The test deserves to be better known. *We find it satisfactory employing the brand of Safranin known as Safranin 'O.'* It is only slowly affected by albumin.

(*Safranine has antiseptic power—see Anthrax.*)

Phospho-Molybdic Acid. For estimating normal urinary sugar. Toluol is useful to preserve. 1 Cc. of specimen is precipitated by 2 Cc. of Phospho-Tungstic Acid reagent made of 2% Phospho-Tungstic Acid in 5% Sulphuric Acid. A dense precipitate is formed. After thoroughly shaking, dilute to 10 Cc. by adding 7 Cc. of Aq. Dest; shake and filter. This filtrate is clear and free from Creatinine and other interfering substances. 1 Cc. of the liquid is heated 6 minutes in a boiling water bath with 2 Cc. of Alkaline Copper solution. Remove and add Phospho-Molybdic Acid solution. Presence of sugar is shown by a deep blue colour. This can be made colorimetric by comparison with a Glucose solution. The amount normally present is very constant. It exceeds 1 Gm. a day on ordinary mixed diet, and the percentage in the urine corresponds curiously closely with that regarded as normal in blood, viz. 0.08 to 0.1%.—R. L. Mackenzie-Wallis, *L. ii./21*, 1003.

4 : 6 Dinitroguaiacol is reduced to intensely coloured 4 nitro 6 amino. guaiacol when heated with solutions of dextrose in presence of sodium carbonate. Reaction is quantitative and lends itself to colorimetric estimation. The reagent is not reduced by other urinary constituents.—*J.C.S.A.* ii./21, 526.

Dinitrosalicylic Reagent for Colorimetric determination of Sugar. is prepared as follows. To 10 Gm. Phenol add 22 Cc. 10% Sodium Hydroxide and make up to 100 Cc. Add 69 Cc. of this solution to 6.9 Gm. Sodium Bisulphite and mix with 300 Cc. 4.5% Sodium Hydroxide, 255 Gm. Rochelle Salt and 880 Cc. 1% Dinitrosalicylic Acid solution.

To 1 Cc. of urine add 3 Cc. reagent, heat 5 minutes in boiling water, cool and dilute to 25 Cc. Compare with standards containing 1, 0.5, and 0.25 mgr. Glucose. Concentrated urines containing over 0.18%, and dilute urines containing over 0.12% of sugar can be considered abnormal.—J. B. Sumner, *Jl. Biol. Chem.*, 1925, 393, per Analyst, '25, 45.

Fermentation Test.—A useful confirmatory test. Prior to conducting determine the specific gravity of the urine as exactly as possible. Then fill a Doremus tube completely with the specimen; place a little fresh yeast in the bend; keep in a moderately warm position for 24 hours. If sugar be present, carbon dioxide will be produced, and the gravity of the urine will fall—each degree of density lost being equivalent approximately to 1 grain of glucose per ounce.

Roberts' Method. After complete fermentation, compare with the original Specific Gravity; a decrease of 0.001 in the Sp. Gr. corresponds to 0.23% sugar. When the sugar content is not less than 0.4 to 0.5%, and

the readings are carefully taken at the same temperature, the method gives fairly exact results.—C.D., Dec. 3/21,72.

Domestic Estimation of Glucose.—The patient requires a urinometer reading 1'000 to 1'040, fresh yeast and a thermos flask. Every night at bedtime he passes his urine into the flask, previously washed out with hot water. A lump of yeast the size of a hazel-nut is added, and the mixture shaken and corked with cotton-wool. In less than 12 hours, at blood heat, any sugar present will have been fermented and the Sp. Gr. will be reduced to a proportional extent. The results are recorded in a squared copy-book.—F. C. Eve, B.M.J. ii./24,504. Cf. Vol. I., p. 649.

Fungi in relation to human pathology.

The "Yeast Method" of detecting Glucose in urine is not specific. Ordinary samples of baker's yeast will ferment Levulose, Maltose, Galactose, Saccharose, Lactose and other Carbon compounds in addition to Glucose. A germ should be used which ferments Glucose only, e.g., *Monilia balcanica* Castellani, or failing this *Monilia Krusei* Castellani, which ferments Glucose and Levulose only. A mycologic method described specially useful for identification of Maltose and Galactose.—A. Castellani and F. E. Taylor, Jl. Trop. Med., July 15, '26,209. See also A. Castellani, L. i./20,847,895, and P. Pietra, Jl. Trop. Med., July 15/27,182.

Renewed investigation of the normal urine sugar problem has brought forth challenges of the presence of Glucose. Lund and Wolf of Addenbrooke's Hospital, Cambridge, proceeded from the thesis that if Glucose is present in urine the products of its fermentation should be detectable when this reaction is attempted, but the most delicate tests failed to demonstrate production of Carbon Dioxide when normal urine was treated with yeast, pointing clearly to the absence of Glucose from normal urine.—Jl. A.M.A. ii./25,1308.

Carbohydrate Test. The char is most distinctive of a saccharine urine.—J. Barker Smith, P.J. ii./24,309; i./25,72,100.

Lævulose

Lævulose reduces Fehling's Solution, ferments with yeast, forms an osazone with Phenylhydrazin like glucosazone. *Vide* also p. 230. Occasionally found in urine alone—more commonly with dextrose.

Pseudo-Lævulose of diabetic and other urines. True lævulosuria or fructosuria may be met with, but it is apparently rare. The lævo-rotatory body is in reality the ketonic acid, isoglycuronic acid which is differentiated from Lævulose by Borchardt's test—the acid is precipitated from an acid solution on saturation with Lead Acetate and the melting point of the parabromphenylosazone. Specimens from 30 cases of so-called lævulosuria and 50 of diabetes in which a lævorotatory substance was present along with Dextrose were examined and in none could any true lævulose be found.

Borchardt's Modification of Seliwanoff's Test consists in treating the specimen with Hydrochloric Acid and Resorcin, making alkaline with Sodium Carbonate and extracting with Ethyl Acetate. With *plant* lævulose the extractive is red in colour, but with urines giving the ordinary Seliwanoff Reaction the watery solution retains the pigment and the extract is yellow.—P. J. Cammidge and H. A. H. Howard, L. i./15,320.

Seliwanoff's Reaction for Lævulose. On warming a solution of Resorcin in 1 part of concentrated Hydrochloric Acid and 2 parts water with Lævulose an intense red coloration is formed and gradually a dark precipitate soluble in Alcohol with a red colour. Glucose, Lactose, Maltose and Pentoses do not give this colour.

Seliwanoff's Reaction for Cane Sugar. The test applied exactly as above gives only a very faint pink on warming. Takes some minutes to form. Using strong hydrochloric acid, the reaction for both is the same. The precipitate in both cases is soluble in alcohol.

Pentose.

Bial's Test (P.G.VI.)—Orcin 1 Gm. in 500 Cc. of Concentrated Hydrochloric Acid containing 25 drops of Ferric chloride Solution.

Method of use.—4 Cc. are heated in a test tube to boiling—then add not exceeding 1 Cc. of the specimen. If pentose present, green colour either at once or shortly. Glycuronic Acid does not interfere.—Mann.

For quantities less than 1% the mixture should be heated in a water bath at 96° C. for two minutes, by this means 0·1% or less can be detected (must not be over heated). We found normal urines with these conditions may give a dull olive green; one should test a normal urine alongside.

Pentose reduces Fehling's Reagent but is not fermentable. It occurs after excess of fruit such as plums. Pathologically it occurs in morphine habit.

NOTE.—Orcin. *Syn.* Methyl Resorcin. Dioxytoluol $1 : 3 : 5$ $C_6H_3(CH_3)_3(OH)_2 + H_2O = 142\cdot080$. White crystals turning pink. Very soluble in water and alcohol. Has antiseptic properties but used mostly as test.

Orcein.— $C_{11}H_{14}N_2O_7 = 500\cdot208$. Prepared from the above. Reddish powder, soluble in Alcohol with red colour, with violet colour in alkalis used as mordant in flagella staining and for elastic tissue in sputum.

Pentosuria.—L. ii./19,117.

Alkaptonuria (Alcaptonuria) (rare), due to presence of Di-oxyphenyl-acetic Acid $C_6H_3(OH)_2CH_2\cdot COOH = 168\cdot064$ Urine reduces Fehling's Solution, and turns brown with alkali. See also Mann *q.v.* also for ochronosis and melanuria. A case.—L. i./07,660. Of 31 cases of alkaptonuria 15 were in children of first cousin marriages.—Sir A. E. Garrod, L. ii./08,5.

Alkaptonuria occurring with pityriasis rubra.—P.R.S.M. Derm. Sect. March, 1910, p. 60. Heredity in.—C. F. Cuthbert, L. i./23,593.

Glycerin.

Glycerin in the urine is claimed to be indicative of pancreatic disease, and to result from the decomposition of fat. Cammidge's Reaction depends on the production of characteristic osazone crystals when the urine is treated with Phenylhydrazin after boiling with Hydrochloric Acid. It is not definitely settled what substance produces the reaction; but it is apparently some carbohydrate-like, possibly some dextrin-like, substance.

Taken in conjunction with clinical symptoms the reaction gives a trustworthy diagnosis of pancreatic disease.—P. J. Cammidge.—B.M.J. ii./10,8. See also *Edn. XVIII., Vol. II., for other refs.*

Later researches, however, have proved that, although the reaction is given in some cases of acute and chronic pancreatitis, as well as in tumours of the pancreas, it is not pathognomic, may occur in other conditions, and may not even be present in pancreatic diseases.

The urine to be examined should be from a mixed twenty-four hours' specimen, and must be free from Albumin and Glucose: if these substances are present they must first be removed. The test can best be carried out in the following manner: To 40 Cc. of clear filtered urine in a small flask add 2 Cc. of strong Hydrochloric Acid, boil for 10 minutes, cool, and add distilled water to make 40 Cc. Neutralise the excess of acid by adding slowly 8 Gm. of powdered Lead Carbonate, allow the mixture to stand for a few minutes, then cool and filter. To the filtrate add 8 Gm. of powdered Tribasic Lead Acetate, filter again and treat with 4 Gm. of powdered Sodium Sulphate: heat to the boiling point and allow to cool. Remove the Lead Sulphate by filtration. Ten Cc. of the clear filtrate are made up to 17 or 20 Cc. with distilled water, 0·8 Gm. of Phenylhydrazin Hydrochloride, 2 Gm. of Sodium Acetate, and 1 Cc. of a 50% Acetic Acid are added, and the mixture again boiled for 10 minutes. Filter while hot and make the filtrate up to 15 Cc. with warm water. When the mixture has cooled, a light yellow, flocculent precipitate forms, which under the microscope will be found to consist of yellow crystals arranged in sheaves and rosettes. These crystals dissolve within a few minutes when treated with a 33% solution of Sulphuric Acid.

This test, when positive, can at best be looked upon as a confirmatory sign in cases in which the clinical symptoms strongly point to pancreatic disease. It has no negative value.—L. Heitzmann, *Urinary Analysis and Diagnosis*, '28. *cf.* also Adrenalin.

Blood and urine examination in pancreatic disease.—P. J. Cammidge and co-workers.—L. ii./20,393.

Chyle gives to urine a milky appearance due to the presence of an emulsion of fat which separates on standing. The urine is acid, Sp.Gr. is usually between 1·015 and 1·020, it is coagulated with Nitric Acid, contains 0·6 to 0·9% protein, 0·8 to 1·8% fat, about 1·5 to 2% Urea, and no sugar. Etiology obscure.—Mann, 1908.

Hippuric Acid.

Syn. BENZOYL-GLYCOCOLL, *vide* Vol. I., p. 8.

Hippuric Acid is excreted daily to extent of about 0.5 to 1 Gm. on mixed diet or it may reach 2 or 3 Gm. on vegetarian diet. It is formed by the interaction of dehydrated Benzoic Acid and Glycocoll in the system. Protein in the intestines produces amino-acids which are oxidised to benzoic acid. **Glycocoll** is a normal product of metabolism, and by this reaction renders the benzoic acid (*inter alia*) harmless,—this occurs, it is thought, in the kidneys 1 of the free acid in 55,000 of water will change Congo red paper to blue, but urine does not cause the change—showing that the Hippuric Acid is present in the combined condition.

Hippuric Acid Estimation.—Heat 100 Cc. of urine with 10 Gm. Sodium Hydrate in a Kjeldahl flask with reflux condenser $2\frac{1}{2}$ hours. Then add Potassium Permanganate 10 Gm in small portions and heat gently for 5 to 7 minutes. The liquid remaining at least pink, cool, add small pieces of ice then Sodium Bisulphite 15 Gm. Still keeping the liquid cool add Sulphuric Acid 1 : 2 *q.s.* to acidify. Shake out five times with Ether. The residue after distilling off the Ether is shaken out with Chloroform. This dissolves out the Benzoic Acid formed. Evaporate and weigh. Multiply resulting acid by 1.468 to obtain quantity of Hippuric Acid.

Indican.

Indican, Potassium Indoxyl Sulphate, $C_8H_7NSO_4K = 251.216$ is excreted in pathologically abnormal quantities in the urine when excessive putrefaction occurs in the intestine. It is tested for as follows. To a test tube $\frac{1}{2}$ full of urine is added an equal quantity of Obermayer's Reagent and a few Cc. of Chloroform. (OBERMAYER'S REAGENT consists of Ferric Chloride 2, Hydrochloric Acid 1000.

This makes a yellow fuming liquid which keeps well. Invert the test-tube a few times to mix. If indican is present in excess the Chloroform will assume an Indigo-blue colour.

Urine of patients taking Potassium Iodide may give colour, and this may obscure a strong Indican reaction. This can be removed by shaking with a little Sodium Hyposulphite, leaving the blue of Indican. Occasionally owing to slow oxidation indigo-red will appear instead of indigo-blue. This gives a colour much like that due to Iodides but it does not disappear when treated with Sodium Hyposulphite. Bile pigments which interfere with the test must be removed by precipitating with Normal Lead Acetate solution and filtering.

Indicanuria is most commonly found in intestinal obstruction and severe intestinal inflammations. It may be present in chronic gastritis, gastric cancer and diminished hydrochloric acid secretion. Decomposition of exudates anywhere in the body as in empyema, bronchiectasis and large tuberculous cavities may cause indicanuria.

Indoxyl. $C_8H_7(NH)OH = 133.064$.

Add an equal volume of hydrochloric acid. Shake and add a drop or two of sodium hypochlorite solution. Blue colour appearing indicates presence. May be shaken into a small quantity of chloroform to render more evident.

Nitrogen.

The quantity in Urine is approximately 0.9% as an average—(90% of this is in the form of urea).

Determination.—Heat 25 Cc. in porcelain basin with 10 Cc. of strong Sulphuric Acid until volume reduced to about 10 Cc. Finally add about 5 Gm. of Potassium Sulphate to the residue in a flask in inclined position with small funnel in neck to act as condenser. Heat until colourless; cool and add very cautiously 20 Cc. water drop by drop, and introduce with utmost care a strong solution of Caustic Soda to alkalinity, for Kjeldahl method by distillation into a known quantity of Standard Acid and ultimate back-titration with alkali, or to near neutralisation by this modified method. Make up volume to 100 Cc.; take of this 10 Cc. = 2.5 Cc. of original urine, and treat this quantity with Hypobromite in a Boremus or other form of Urea Apparatus.

In this way 24 Cc. of moist Nitrogen = approx. 0.028 Gm. Nitrogen or 0.034 Gm. Ammonia, or 0.06 Gm. Urea. *q.v.* for further information.

Folin and Denis' Method of Estimating Total Nitrogen.

Modified Nessler Reagent—Folin and Denis criticise the composition of Nessler's Reagent as being excessively alkaline and containing too little Potassium Iodide. They dissolve Potassium Iodide 75 Gm. in warm water 50 Cc. add Mercuric Iodide 100 Gm. and stir. Dilute with water 400 or 500 Cc. filter and make up to 1 litre. To 300 Cc. of this Double Iodide solution add 200 Cc. of 10% Sodium Hydroxide, 500 Cc. of water and mix. This final solution contains 2% Sodium Hydroxide, which is preferable for Nesslerising Digestion Mixtures of samples of Urine.

15 Cc. of this Reagent added quickly to the digestion mixture will yield *clear* mixtures with as large amounts of ammonia as are met with in the method (0.7 to 1.6 mgr. Ammonia-Nitrogen).—O. Folin & W. Denis, *Jl. Biolog. Chemistry*, 1916, p. 473, *et seq.* Further data see 18th Edn. Vol. II., p. 422.

Ammonia.

In urine may be estimated by distillation and Nesslerisation of the distillate or by aid of Volumetric Acid, as above.

The average amount of total ammonia in urine is 0.3% by weight.

Ammonia excretion varies during 24 hours—it is greatest during the night. Bodily exercise by producing acids increases output as also does consumption of fat (usually seen after interval of 1 to 2 days).

In fevers, malignant disease, diseases of the liver, ammonia is increased. In pernicious anæmia the amount may be considerably above or it may be rather below the average.

For Malfatti's and Folin and Denis' Methods, see Edn. XVIII., p. 423-424.

Phosphates.

(Mean content is 0.15 to 0.2% P_2O_5 .)

These are estimated by means of a **Standard Uranium Nitrate Solution**, prepared by dissolving 35 Gm. of the Nitrate in 900 Cc. of water, and standardising it against 50 Cc. of a solution of 5.042 Gm. of pure Sodium Phosphate (*B.P.*'14) in 1 litre of water 5 Cc. of a solution of Sodium Acetate 100 Gm., with 100 Cc. of Acetic Acid in water *q.s.* to 1 litre is added, both in standardising and in the estimation of the sample of urine. A few small crystals of Potassium Ferrocyanide on a white tile serve as an indicator.

The estimation is now seldom conducted. Details Edn. XVIII., Vol. II. p. 424.

Joulie's Ratios.—The so-called alkalinity of the blood is due to the presence of Bicarbonates which are chemically Acid Salts, so that in spite of the alkalinity to litmus the blood may according to Joulie be viewed as an acid fluid. The acidity due to Sodium Acid phosphate is masked by the excess of the Bicarbonates. The blood contains in solution Calcium Phosphate and Magnesium Phosphate, and seeing that these are precipitated in alkaline or even faintly acid solution, this is considered another point in favour of the view that blood is acid in reaction. Bicarbonates are practically absent from the urine. A treatment was evolved based on determination of the acidity of the urine (according to Joulie, due to Sodium Acid Phosphate).

Joulie compares the degrees of acidity of urines for equal amounts of Solids in specimens as indicated by the increase in Specific Gravity over that of water, and expresses the result in percentage, *e.g.*, if the Sp. Gr. be 1.015 and the acidity 0.505 (in terms of H_2SO_4 per litre), then an excess of density equal to 100 would give

$$\frac{0.505 \times 100}{15} = 3.36 \text{ as Ratio of Acidity ('R.A.')}$$

It is then obviously possible to find a Urine with Specific Gravity lower, *e.g.*, 1.005, showing a lower acidity per litre. *e.g.*, 0.308, which is in reality more acid when we eliminate the increase of water—thus

$$\frac{0.308 \times 100}{5} = 6.16 \text{ as 'R.A.'}$$

The determination of acidity per litre is, therefore, considered fallacious. The average R.A. in health is 4.55. A ratio above is hyper-acid, and below is hypo-acid. The latter condition is much more common, due to failure of hepatic function.

In vegetarian diet the excess of alkalis appearing as Carbonates in the urine will produce an alkaline reaction.

To relieve hypo-acidity with the resultant pathological deposition of lime salts, and the production of phosphatic gout, dilute Phosphoric Acid should be given. (Other Acids would have the same effect but they coagulate Albumin and are not well tolerated by the stomach.) Further Phosphorus is a normal constituent of bones, plasma, blood, etc.

The daily total average loss of Phosphoric Acid is estimated at 3 Gm. in the urine and 1.5 Gm. in the fæces—total 4.5 Gm.

To raise the acidity of the urine (and hence of the blood as Joulie claims) large amounts of Phosphoric Acid have to be given.

Sodium Acid Phosphate would be indicated where there is deficiency of H_3PO_4 accompanied by a mild hypo-acidity—usually up to 5 Gm. per diem is given.

The Ratio of Phosphoric Acid (R.P.) to excess of density of urine over water is on an average 11 to 11.5. If above this, the condition is called hyper-phosphatia.

Normally $\frac{R.P.}{R.A.} = 2.45$ (Joulie's co-efficient or Acido-phosphoric ratio).

PHOSPHATIA is applied to a condition of abnormal amount of phosphates and requires the prefix hyper or hypo to indicate excess or deficiency. According to Joulie if the R.P. is *excessive*, it is treated by diet rich in phosphates—gruyere cheese, haricot beans, mutton, beef, white cheese, eggs, cereals, milk enumerated in order of preponderating percentages). If R.P. *deficient* this means excessive phosphoric excretion has *preceded*, therefore also administer phosphates; the kind of Phosphate to give depends on the R.A.

If the R.A. is *normal*, a neutral phosphate must be given. **Sodium Sesquiphosphate** as described Vol. I., p. 777, has been suggested and is specially prepared.

Hyper-acidity will rapidly yield to the ordinary Sodium Phosphate, *e.g.*, in the form of Effervescent Sodium Phosphate.

Purins.

Of the known Purin bodies, Xanthin, Hypoxanthin, Adenin, Guanin, Caffeine, Theobromine, are met with in food, and Uric Acid, Xanthin, and traces of Methylxanthin are found in urine.

(Caffeine, Theobromine, etc., are pure cerebral stimulants. They do not impair the quality of work.—Prof. Wild, L. ii./20,53.)

They all contain the grouping C_5N_4 —Xanthin is dioxypurin, Uric Acid is trioxypurin. Uric Acid is in the largest proportion of the purins—about 10 to 1 of the others.

There is no special therapeutic effect in a purin-free diet.

Guanidine Metabolism.—Its action on administration is to produce symptoms identical with those seen after removal of the parathyroid glands. Correlation needed in terms of metabolic change of *Arginine* with its Guanidine nucleus, the Guanidine bases themselves and creatine with its methylated group.—Abst. Ann. Rep. Chem. Soc., 1919 (Vol. XV.), p. 152.

Guanidine, preparation of. —E. A. Werner & J. Bell, J.C.S. Oct. '20, 1133.

Suggestion that the Guanidine bases are in part or wholly responsible for the cause of the hypertension so often concomitant with nephritis, owing to the fact that Guanidine constricts the capillaries.—per Jl.A.M.A. ii./25,1671.

Pus.

Microscopic examination is essential when pus cells are found in the centrifuged deposit: count should be made of the number of cells per cubic mm. A drop of the fresh uncentrifuged urine is examined in a Fuchs Rosenthal counting chamber. A few leucocytes may be present in the urine in health, and as the result of several thousand tests C. E. Dukes has shown that 0-10 leucocytes may be present per cubic mm. in the urine of healthy people, and he suggests as a definition of pus "more than 100 leucocytes per cubic mm." The intermediate zone between 10 and 100 is described as the zone of excess of leucocytes. Degrees of pyuria have been defined by Dukes as follows:—100-1,000 Pus, 1,000-10,000 Pus +, and 10,000-100,000 Pus ++.

Mucus threads are sometimes found in the urine of male patients who have had gonorrhœa several years previously. These appear as a long thread-like process of mucus uniting chains of pus cells. They are common after prostatic massage and may be present only in the first morning specimen.

Cholesterin is rarely found. It is usually derived from a collection of pus that has been retained in a cavity for some time, ultimately discharging into the urine.

To separate cholesterin extract the specimen with alcohol-free Ether. Purify the residue on evaporation by dissolving in strong alcoholic potash, evaporating, extracting again with Ether, and this again with boiling alcohol—rhombic plates.

Chloroformic solution of Cholesterin with Sulphuric Acid gives a red to purple colour. An Alcoholic solution so treated gives red to blue.

Cholesterin crystals are found in the urine, in diabetes, in cystitis, Bright's disease, pyonephrosis, epilepsy, in tabes and lipuria, and in fatty degeneration of the kidneys.

Renal Function Tests.

Of the numerous tests devised for estimating the functional activity of the kidneys the following have proved the most reliable in practice.

(1) **Systematic examination of the urine**, including the record of the total quantity passed each day, the Sp. Gr., the presence of albumin, blood, and pus, and the presence of casts. If the patient is on a standard diet and accurate daily quantitative tests can be made, useful information can be obtained from quantitative tests of urinary constituents, particularly of the urea and chlorides in the urine, but this method has only a limited applicability in practice. The following table from "Recent Advances in Medicine" (4th Edn., p. 23), by Beaumont and Dodds gives figures obtained at the Middlesex Hospital.

Table showing analyses of twenty-four hours' urine of typical cases of renal inefficiency.

Case.	Vol Cc.	Albu- min per 1,000	Urea Gm.	Uric Acid Gm.	Creati- nin. Gm.	Total N. Gm.	Chlorides Gm.
Normal men ..	1,500	—	30	0.6 to 1.2	1 to 1.25	14 to 16	10 to 15
Acute Nephritis	300	20	7	0.2	0.8	6	1.7
Chronic intersti- tial Nephritis .	3,000	0.5	15	0.6	0.9	8	14.8
Large white kidney ..	1,000	10	14	0.72	0.85	7	1.7
Small white kidney ..	1,800	12	12	0.84	0.79	6.4	0.9

(2) **Blood Tests.** **Blood Urea Estimation** is of chief value in suspected cases of nitrogen retention, particularly in the diagnosis of uræmia and urinary obstruction. 5 to 10 Cc. of blood are taken from a vein. The whole blood, oxalated plasma, or serum may be used for the test. The normal figure is 20 to 40 mgr. of urea per 100 Cc. of blood. Urease contained in Soya Bean is used. It converts Urea quantitatively into Ammonium Carbonate, but has no effect on other nitrogen constituents. (The hydrolysis is complete in 15 minutes.) The Ammonia from the Ammonium

Carbonate is liberated by alkali and passed into standard acid. Caprylic Alcohol is used in conjunction with the Soya Bean flour. See Urea Chapter for further details.

Blood of normal individuals may contain 15 to 40 mgr. Urea per 100 Cc. of blood—over 45 mgr. is suspicious. If over 50 mgr., kidneys are inefficient. Discussion of Renal Efficiency Tests. H. MacLean, B.M.J., ii/21, 4-5.

Nitrogen determination by direct Nesslerisation.—To 5 Cc. of fresh oxalated blood in a 50 Cc. flask add about 0.1 Gm. soy bean meal in the form of a 1% suspension. Allow to stand 1 hour. Then add 25 Cc. water and 2 Cc. *m*-Phosphoric Acid (25%) and make up to volume. Mix thoroughly, stand 45 minutes and filter. To the filtrate add 0.5 Gm. Blood Charcoal, shake and filter. In the case of normal blood place 10 Cc. of the last filtrate (= 1 Cc. of blood) in a 25 Cc. flask. Add 5 Cc. special Nessler Solution (*q.v.*), make up to volume, mix and compare at once against 0.25 mgr. ammonia nitrogen Nesslerised in a 50 Cc. flask (using 10 Cc. of Nessler Solution).

If only 2 Cc. of blood are available proceed exactly as above (including coagulation in a 50 Cc. flask) except that 20 Cc. of the final filtrate (= 0.8 Cc. of blood) is taken for Nesslerisation.

Range in nine cases was from 12 to 75 mgr. Urea Nitrogen per 100 Cc. of blood.—O. Folin & W. Denis, *Jl. of Biolog. Chemistry*, 1916, p. 505.

See also our pp. 62—64.

The urea in the urine (see *Urea*) should be estimated at the same time. In marked cases of uræmia the blood urea is often (but not invariably) above 100 mgr. In interpreting figures between 50 and 100 mgr. the limitations of the test must be kept in mind, namely, the fact that any disease such as diarrhoea or diabètes, which leads to severe anhydræmia tends to raise the blood urea. Similar effects are produced by a failing circulation due to a fall in blood pressure. Therefore it is often difficult to assess the value of the test in patients who are very ill. In general it may be said that marked nitrogen retention and therefore high blood urea occurs in chronic interstitial nephritis and with urinary obstruction. Little or no retention is found in parenchymatous nephritis until the terminal stages.

Blood Cholesterol in chronic parenchymatous nephritis. The estimation of this is of value particularly for checking treatment. Normally the blood cholesterol is about 0.1% but may rise to 0.3% in parenchymatous nephritis. With suitable treatment the blood cholesterol falls as the case improves clinically.

(3) Elimination Tests.

The **Urea Concentration Test** is the most popular. The principle is to give a large dose of urea (15 Gm.) *per os* and observe how rapidly the kidney removes the excess. The test is best carried out first thing in the morning.

Technique.—The patient is allowed no food or drink after 10 p.m. the previous night. At 5.58 a.m. the bladder is emptied completely and this specimen of urine marked '0.' At 6 a.m. he takes the following mixture, Urea 15 Gm., Tincture of Orange 1 Cc. and Water 100 Cc. At 7 a.m. he empties his bladder completely, this specimen being marked '1.' At 8 and 9 a.m. he passes urine again, these specimens being marked '2' and '3' respectively. The total quantity of urine passed at 7, 8 and 9 a.m. must be measured. This should not exceed 120 Cc. in No. '1' and 100 Cc. in Nos. '2' and '3.' If more than this is passed it indicates that the urea has a diuretic action and a low urea concentration may not necessarily mean a poor renal function.

Normally the concentration of urea in one or other specimen is at least 2.5 or 3%. In renal inadequacy it is below 2%.

The chief limitations of the test are that in the hydræmic type of nephritis with chloride retention it may give normal results

even when the patient is very ill, because in this disease there is not necessarily any nitrogen retention. Nor is the test always reliable in cases of enlarged prostate.

Dye Excretion Tests are of chief value in comparing the functions of *each kidney separately*, the urine being collected by ureteric catheterisation. The *Indigo Carmine* and *Phenol Red Methods* are dealt with, pp. 62-64.

Significance of renal function tests.

The tests are of chief value in certain surgical conditions, in the albuminurias of pregnancy and in the diagnosis and prognosis of medical cases of kidney disease. In surgical cases of obstruction the blood urea has been found to be the most useful test of kidney function. A blood urea content above 60 mgr. per 100 Cc. contraindicates prostatectomy in one stage. In other types of surgical cases the dye excretion tests are most satisfactory and are usually performed by the surgeon himself.

In cases of albuminuria in pregnancy with clinical symptoms such as headache, vomiting and œdema, as in nephritis toxæmia (de Wesselow) there is marked nitrogen retention, with a blood urea above 40 mgr. per 100 Cc. and a high blood pressure. In threatened eclampsia there is albuminuria, diminished urea output and frequently an increased blood urea, but the imminence of eclampsia cannot be judged from the amount of nitrogen retention.

In medical cases of kidney disease renal function tests are often useful but it must be borne in mind that obstruction to urinary outflow produces much greater nitrogen retention than severe kidney disease. Blood analysis is particularly useful in checking the effects of diet in cases of nephritis with nitrogen retention. Similarly in parenchymatous nephritis the value of treatment can be assessed by the reduction in blood cholesterol. Whatever tests are performed their value must always be weighed in the light of information gained from general clinical examination, the blood pressure and condition of the arteries.

References.

With regard to treatment, Epstein's advice that *patients suffering from marked œdema or ascites resulting from parenchymatous nephritis should receive liberal protein diet is substantiated. Large doses of UREA given in such cases resulted in disappearance of the dropsy. 30 Gm. or more per diem persevered with.* Bad cases have been cured.

In interstitial cases where nitrogen retention is more or less well marked protein especially meat is on the whole contraindicated. Milder cases are, however, probably not benefited by strict dietetic limitations. The whole question of protein diet in kidney disease requires much investigation.—H. MacLean & A. E. Russell, L. i./20, 1305, and L. i./25, 1213, Pr. Jan., '26, 67.

The average urea content in urine was found to be 1.6% in the case of patients under observation in hospital. When the kidneys are damaged the concentration falls below that figure. That the specific gravity of the urine is consistently low in advanced granular kidney disease is a well recognised fact. Salt retention is a characteristic of the œdematous or tubal type of nephritis just as urea retention is characteristic of the chronic interstitial or cirrhotic type.—C. R. Box, B.M.J. i./20, 356.

Albuminuria in relation to LIFE INSURANCE.—F. Parkes Weber.—B.M.J. i./21, 78.

Renal function tests, Discussion of. The blood urea test preferred to Phenol Red. Less than 50 mgr. of Urea per 100 Cc. of blood has a favourable prognostic significance. If over 50 mgr. non-protein diet called for. If over 100 mgr. prognosis grave.—L. ii./21, 337.

A blood urea content as high as 300 or even in rare instances 400 mgr. per 100 Cc. is not incompatible with recovery in an acute case of nephritis, and even in chronic types in which the capacity is of necessity less, a blood urea content of 100 to 200 mgr. does not necessarily imply a speedy death. Inorganic phosphate estimation of value. Phosphorus is more definitely connected with symptoms of true uræmia than is the retention of urea.—O. L. V. de Wesselow, L. ii./23, 163.

Interpretation of the Urea Test figures important. A high blood Urea content may be produced by causes acting outside the kidneys altogether. It is really dependent on the cardiac condition and not on the kidneys. The figure for blood Urea does not help much in forming an opinion as to condition of the kidney, unless one is certain from other symptoms or tests that the case is really one of nephritis.—Prof. H. MacLean, L. ii./23,1100.

In diabetes associated with renal disease there was a marked inability to concentrate Urea (MacLean's Test). The determination is of more value than that of blood-urea in estimating the function of the kidney.—E. Wordley, L. i./25,655.

Diastase Test is not found satisfactory in practice. Details Vol. II., 18th Edn., p. 378. Urines should be brought to a standard H ion concentration, preferably the optimum pH 6·7. Low values indicate nephritis as a rule.—A. F. Sladden, L. ii./22,68.

Diastase Estimation in urine and blood; useful in confirming other renal efficiency tests.—G. A. Harrison and R. D. Lawrence, L. i /13,169.

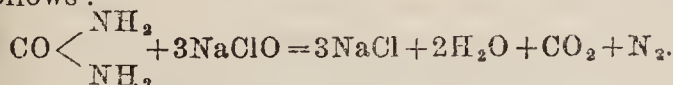
Sodium Benzoate Test.—After taking 2·4 Gm. with 300 Cc. of water, normally 70 % is excreted in the urine after 2 hours and 90 % after 3 hours, as Hippuric Acid.—Y.B.P., '24,59.

See also **Urea Estimation chapter.**

Urea.

Average content in the urine is 2·5 to 3%, or about (in health) 500 grains (33 Gm.) per diem; it may range between 15 and 40 Gm. The majority of methods are based on the decomposition of Urea into nitrogen, carbon dioxide, and water when treated with sodium hypobromite. The carbon dioxide is absorbed by the excess of alkali present, and the nitrogen can be measured, from which, on reference to tables, the percentage can be found—theoretically 1 Cc. of nitrogen at 0° C.=0·0027 Gm. approximately of Urea. In the process about 8% of the total nitrogen is suppressed, but the increase in volume of the gas due to the room temperature (taken as 18° C.) and the vapour tension (the gas being measured moist) has been found to almost exactly compensate for this loss in practice.

Sodium Hypobromite we found is *more accurate* than Sodium Hypochlorite, which was at one time used for the purpose—the Nitrogen being evolved more rapidly and completely. Sodium Hypochlorite decomposes Urea as follows:—



With Hypobromite the reaction is analogous.

The chief cause of low results in the Hypobromite method appears to be the presence of undecomposed Urea, this difficulty being obviated by carrying out the reaction in warm solution.—J.C.S., A. ii./23,591.

A further explanation which has been given for the decomposition of only 90 % of the Urea present (using Hypobromite) is that Sodium Cyanate is formed.—M. D. Donald, C.D. ii./25,894. The fact remains that in the Urea apparatus devised by the author—a modification of Squibbs'—the results are very close to theory and quite adequate for clinical research.

Sodium Hypobromite Solution. *Syn.* PAYNE'S REAGENT.

Caustic Soda 100 Gm., Distilled Water 250 Cc. Dissolve, cool, and keep iced while adding *guttatim* Bromine 25 Cc.

Mix and dissolve. This solution is used to estimate the amount of urea in a given quantity of urine. On adding the solution, nitrogen is evolved from the urea and is measured in a **Doremus Ureometer**.

It is better to keep the bromine separate; it may be used in sterules containing 1, 2, 3, and 4 Cc. respectively; 1 Cc. of bromine should be added to 11 Cc. of the solution as required. In place of these,

Liquor Bromi—Bromine 1 Cc., Potassium Bromide 1.5 Gm., Distilled Water *q.s.* to 11 Cc. (= 1 in 11) may be used in equal quantity to the soda solution.

In the **Urea Apparatus** arranged by the author the Nitrogen evolved displaces an equivalent volume of water and the content of Urea is easily read off from the table.

See also Nitrogen chapter, antea.

Urease method of estimating Urea. Mix 25 Cc. of the urine with a pinch of powdered Soy Bean Flour (2 to 3 Gm.). Allow to stand overnight covered with a small layer of Xylol or Benzol. Render the liquid alkaline with strong Sodium Carbonate solution and distil into Standard Hydrochloric or Sulphuric Acid by Kjeldahl's procedure. Urease only attacks *urea*, 1 molecule of urea producing 1 molecule of Ammonium Carbonate $(\text{NH}_4)_2\text{CO}_3$, and there may be present a small amount of Ammonium Salts in addition to free Ammonia. For accurate work these must be estimated separately.

Urease preparation. Cover 200 Gm. of finely powdered Soya Bean with 1,000 Cc. water and keep 6 hours. Treat the filtrate with 96% Alcohol (400 Cc. ?), as long as precipitate forms. Collect and dry slowly and add Lactose *q.s.* to 100 Gm. Keep product dry.—Y.B.P. '23,154; '24,142.

Experiments on with various temperatures.—J.C.S.A. i/20,103.

Urease found in melons, beans and pumpkins.—per J.L.A.M.A. ii./25,1007.

Urea Nitrogen determination by direct Nesslerisation:

UREASE is used as above for hydrolysis of the Urea, either in form of the enzyme or as soy bean meal. It decomposes urea quantitatively and does not affect other constituents of Urine.

Place 1 Cc. of the Urine in a 100 Cc. graduated flask. Add 0.1 to 0.25 soy bean meal in the form of a 1% suspension. Allow to stand for 1 hour at room temperature, or 15 minutes at about 50° C. Add 25 Cc. of water and 1 Cc. *m*-Phosphoric Acid Solution (25%) and mix, then add 1 Gm. pure Blood Charcoal, shake, make up to volume, mix, and filter.

(The soy bean meal suspension is made thus:

Rub 5 Gm. with water 15 Cc. to a smooth paste. Add more water *q.s.* to about 400 Cc. Add 100 Cc. alcohol. 10 to 15 Cc. of this are used. It keeps good about 2 days.)

Place 5 to 20 Cc. of the filtrate in a 100 Cc. graduated flask. (The amount taken should contain 0.7 to 1.3 mgr. ammonia nitrogen.) Dilute to 60 or 70 Cc. Nesslerise with the modified Nessler Reagent, *v. p.* 382, and compare with standard (1 mgr. of Ammonia Nesslerised in another 100 Cc. flask).

Range in specimens examined 3.4 to 10.16 Gm. Urea Nitrogen per litre.—O. Folin & W. Denis, *Jl. Biolog. Chemistry*, 1916, p. 501 *et seq.*

The determination of minute quantities of urea by hydrolysis with acid at 150° C. followed by Nesslerisation.—*Jl. Biol. Chem.*, '25,275. Analyst, '26, 154.

NH.CO

Alloxan.— $\text{CO} < \begin{matrix} \text{NH.CO} \\ \text{NH.CO} \end{matrix} > \text{CO}$ Mesoxalylurea, is an oxidation product

of Urea. It can be made by introducing Urea in small portions at a time into strong Nitric Acid.

URÆMIA AND HYPERPIESIA. The former name is a misnomer unsupported by experimental investigation. The relationship of uræmia and hyperpiesia is easily settled. Hyperpiesia reveals in its advanced stages each and every manifestation met with in uræmia. The poisons circulating in the blood, which produce hyperpiesia or symptoms cannot be described, but they are there and are in no way expressive of defective action of the kidneys.—H. Batty Shaw, *L. ii.*/21,1307.

Andrewes' simplified Diazo Test for Uræmia is carried out by removing the proteins from the serum by adding 2 vols. of Absolute Alcohol and centrifuging or filtering. To 4 vols. of the filtrate is added 1 vol. of Diazo

reagent—this is the same as that used in Van den Bergh's Test, *q.v.*,—and the mixture boiled for $\frac{1}{2}$ to 1 minute when 40% Soda solution is added drop by drop, shaking after each addition. The test is positive only when a deep pink or cherry red colour is seen, which colour may last only for a few seconds.—G. A. Harrison and L. F. Hewitt, B.M.J. ii./27, 1138.

Uric Acid, *Syn.* Lithic Acid.

$C_5H_4N_4O_3 = 168.064$. **Manufacture.**—Mix Guano 28 lbs. with 3 gallons of water. Acidulate with commercial Hydrochloric Acid. Boil, filter, and wash to remove calcium and ammonium salts (Phosphates and Oxalates). Boil the residue with Sodium Hydrate *q.s.* in 5 gallons of water—filter. Wash residue well and acidify filtrate with Hydrochloric Acid. Uric Acid separates and is filtered off. Redissolve in Sodium Hydrate, precipitate again with acid, wash and dry.

When pure, Uric Acid is in white crystals, very slightly soluble in water insoluble in alcohol and ether

Heated to dryness on a water bath, with a little Nitric Acid or Potassium Chlorate and Hydrochloric Acid in a white dish, cooled, and a little Ammonia solution added gives a red colour.—The **Murexide Reaction**.

The average Content in the urine is 0.05 to 0.06%, but no relation has been found between amount of Uric Acid in the urine and health of rheumatic patients.

Hopkins' Method.—To 100 Cc. of sample add about 30 Gm. Ammonium Chloride in powder, dissolve as completely as possible, or a small quantity may remain undissolved, add a little ammonia to neutralise and allow to stand 10 minutes. Filter off the precipitated Acid Ammonium Urate, wash with Saturated Ammonium Sulphate solution* and rinse off the precipitate from the filter with water to 100 Cc. Add 20 Cc. Concentrated Sulphuric Acid to raise temperature of the liquid to about 60° C., or, if necessary, warm to that temp. Titrate with $N/_{20}$ Potassium Permanganate (1.58 Gm. in 1 litre), taking as end-reaction the point at which the Permanganate ceases to be instantly decolourised. Each Cc. of the Permanganate Solution = 0.00375 Gm. Uric Acid.

The **Gowland-Hopkins' method** is as above to*, then proceed as follows:—Wash off the precipitate into a small beaker with a jet of hot water, add a little hydrochloric acid, and heat to just boiling. Allow to stand two hours in the cold. Collect the separated Uric Acid measuring the filtrate at the same time, for which an allowance of 1 mg. must be added on to the final result for every 15 Cc.; it need not exceed 20 to 30 Cc. Wash the uric acid crystals with a little distilled water, rinse off the filter with hot water, warm with sodium carbonate till dissolved and make up with water to 100 Cc. Add 20 Cc. Sulphuric Acid and titrate with Permanganate as above adding slowly towards the end of the reaction, the finish being the first appearance of a pink colour which is permanent for an appreciable interval. Previously the disappearance of the colour is instantaneous.

Phospho-Tungstic Acid Test ($H_3PO_4 \cdot 12WO_3 + Aq$) for Uric Acid. A rapid approximation.

Mix about 10 Cc. of urine with 3 Cc. of Liquor Potassæ, add 20 drops of Solution of Phospho-Tungstic Acid (20% Solution). Uric Acid causes a blue colour which varies in depth with proportion present. The method is not applicable for anything approaching an accurate colorimetric estimation as the colour fades rapidly. Use a standard for comparison of 1 in 50,000 Uric Acid.

The test can also be conducted by heating the urine with Liq. Potassæ and a 5% solution of Phospho-Tungstic Acid which gives a lilac colour. The intensity can be compared with that given by a Standard Solution of Uric Acid 1—1,000.

Uric Acid in Blood.—Method of estimation by means of the **Hellige Colorimeter**.—See 'Blood and Urine Chemistry.'—Gradwohl & Blaivas, 1920.

Uric Acid content both of blood serum and of corpuscles is twice as great in gouty conditions as in normal health.—J.C.S. A. i./1922, 1086.

Excess of uric acid in the blood may be etiologically related to eczema and allied dermatoses.—J. F. Schamberg and H. Brown, *per. Jl. Trop. Med.*, Nov. 15/23, 343.

Sodium Bi-urate. $C_5H_3NaN_4O_7 = 190.053$. May be prepared by neutralising Uric Acid with Sodium Carbonate. Various opinions have from time to time been expressed as to whether the crystals are the cause or effect of the inflammation in arthritis.

Methods of correlation in urine examination. Certain substances (Sodium, Potassium, Chlorine) are excreted with water, hence through the glomeruli. Others (Urea, Uric Acid, SO_3) are excreted independent of the water, therefore, presumably, through the tubules. There is no indication that Uric Acid is excreted as Sodium Urate but rather as Calcium and Potassium Urate.—C. P. White, L. i./22,369.

During pregnancy and delivery rather low values for Uric Acid in the blood were found, the average being 2.74 mgr. per 100 Cc.; may increase slightly after delivery. In eclampsia, Uric Acid is always considerably decreased.—per JI.A.M.A. ii./25,861.

Acidity of Urine.

The **Acidity of Urine**, due mostly to the Sodium Acid Phosphate, is determined by titration with Decinormal Alkali using Phenolphthalein as indicator. Each Cc. of this standard solution = 0.012 Gm. of Sodium Acid Phosphate. Acidity is frequently reported in terms of the number of Cc. of this Alkali per 10 Cc. of Urine, *e.g.*, 3 Cc. = 3°, and the **Alkalinity** similarly.

The urine of half-a-dozen individuals in health was found by us to have the following 'degrees' of acidity—0.8°, 0.9°, 0.9°, 4.4°, 5.5°, 7.2°.

It was noticeable that this gradation did not correspond with the acidity as shown by delicate litmus paper—on the contrary, the two with 0.9° were distinctly different.

Acidity of Urine. There are at least two acidities, one reacting to Methyl Orange, the other to Phenolphthalein. The acidity responding to Methyl Orange is not constant like the other.—E. & E. Pittarelli, per Y.B.P. 1919, 54.

The acidity of the urine, according to Joulie, is dependent on the 'acidity' of the blood (due to acid phosphates). *Cf. Joulie's Ratios. antea.*

Reaction and Disease.

People may be divided into acid, normal and alkaline constitutions. In tuberculosis a definite alkaline incidence (shown by urine examinations) is necessary for activity, improvement being obtained on increasing acidity, by exercise, and by acid-producing foods, *e.g.*, meats and fats. Arteriosclerosis, rheumatism and high-blood pressure are caused by excessive acid production and cases are exceedingly tolerant of alkaline mixtures. Observations have shown that arteriosclerosis and allied diseases are rarely seen in tuberculosis cases.—H. A. Ellis, Conf. Tub. Soc. of Gt. Brit., Bristol, Mar., 1923; see also Med. Jl. & Rec., Apl. 6/27.

BACTERIOLOGY OF THE UROGENITAL TRACT.

On finding pus in the urine it should be examined bacteriologically to ascertain the nature of the infecting agent. Radiological examinations may be necessary also to rule out the question of calculus.

In women a catheter specimen of urine is required, but in men it is possible to obtain a suitable specimen without catheterisation if the glans penis is carefully cleaned and the patient instructed to pass the first portion of urine into an ordinary receiver and the next portion into a sterile wide-mouthed bottle. The specimen must be despatched to the laboratory immediately after collection.

The following are the chief bacteria responsible for infections of the genito-urinary tract.

Gonococcus.

In the male the gonococcus causes an acute urethritis in the first place. There is no difficulty in the recognition of this intracellular diplococcus in properly stained films made from the urethral discharge in the early stages of the infection. In the later stages of infection the gonococcus is not easily found and a more thorough examination is necessary. The following procedure is recommended in chronic cases and particularly when the patient

seeks advice as to infectivity when contemplating matrimony. The patient should come for examination in the early morning with instructions not to pass urine till investigated. Films are made from any discharge in the urethra, and the urine passed and examined by naked eye for prostatic threads. The urine should be centrifugalised and the deposit stained. (For the staining methods see *Bacteriological Notes Chapter.*) The patient should then be placed in the knee elbow position and the prostate massaged. The prostatic fluid is collected and examined by films and cultures on serum agar. If a purulent morning discharge is absent, if there is no pus in the urine and if the prostatic fluid is clear and contains only mononuclear cells, the patient, in the absence of clinical signs and symptoms is probably free from gonorrhoea.

The examination of the female genito-urinary tract for gonococci is less commonly successful, even in the acute stage, and greater reliance should be placed on the cultural than on the film results. (*Panton and Marrack.*)

Before pronouncing a woman free from infection at least three tests should be made. Films and cultures should be taken from the interior of the urethra, from the cervical canal after passing a speculum, from the vagina, and if clinically infected, from Bartholin's duct.

Bacillus Tuberculosis.

Films from the centrifuged deposit should be stained by the Ziehl-Neelsen method and decolourised with Methylated Spirit as well as Sulphuric Acid. Repeated examinations may be necessary. It is not worth while spending time on a specimen which does not contain pus. The final court of appeal in doubtful cases is guinea pig inoculation.

Bacillus Coli.

In acute cases with vesical or renal symptoms the urine is usually turbid due to the presence of blood, pus and bacteria. *B. Coli* are present to the extent of thousands per cubic mm. of urine.

In more chronic cases the symptoms are less severe or even inconspicuous but microscopic examination shows pus and bacteria. The urine is usually acid. Bacteriological tests should be undertaken as soon as possible after the specimen has been collected. *For further procedure see Bacteriological Notes Section.*

The presence of *B. Coli* in the urine does not prove that these bacteria are the actual cause of the infection because a secondary infection with *B. Coli* is often super-imposed on some other lesion such as tuberculosis or calculus.

Bacillus Typhosus.

The typhoid bacillus is excreted in the urine in the later stages of typhoid fever, and it may exist in the urine without causing symptoms. Such carriers are a great source of danger to others.

Cocci.

Any of the pyogenic cocci may be found in the urine and give rise to acute inflammations. When on repeated examination of the urine, *Staphylococcus albus* alone is recovered the possibility of calculus must be kept in mind. *Streptococci* are often recovered from chronic prostate infections.

A Portable Urine Test Case is arranged, containing the apparatus and reagents for the qualitative examination of urine for Sp. Gr., albumin and glucose, also a 'Complete' Test Case for full quantitative investigations.

BLOOD EXAMINATION.

Blood Corpuscles.—The red blood corpuscle has an average diameter $7.5 \mu = \frac{1}{3388}$ inch. It is discoid in shape with indentations in the two sides. Occasionally it is smaller, e.g., $6 \mu (= \frac{1}{4200}$ inch). Price-Jones determined in normal human blood diameter to be 6μ to 8.75μ —with an average of 7.4μ , whilst in pernicious anaemia the diameter varied from 4μ to 11.75μ , and the average diameter of five successive 100 cells was 8.0μ .

In disease it may reach 8 to $10 \mu = \frac{1}{3175}$ to $\frac{1}{2540}$ inch, i.e., ANISOCYTOSIS, or irregularity in size; further in disease the corpuscles may exhibit POIKILOCYTOSIS, i.e., irregularity in shape. In

examination of films **VACUOLATION** should be noticed, as also irregularity in staining (**POLYCHROMATOPHILIA**). With regard to abnormal red cells—these are mainly of two kinds, (1) those like normal cells without nuclei, (2) nucleated. The group (1) where they have special designations have names ending in *cyte* (*microcyte*, *megalocyte*, etc., based on the type of the normal corpuscle which is called *erythrocyte*) whilst the nucleated forms have names ending in *blast*. In this group are *normoblasts*, *megaloblasts*.

For details of white corpuscles *v. p.* 396.

Precipitin Test for Blood.—Precipitins are formed when the serum of one kind of animal is introduced into the body of another species, *e.g.*, the serum of a horse injected into a goat causes the serum of the goat to be capable of forming a precipitate with normal horse serum.

In using the test for forensic purposes a rabbit is injected with human blood serum. The serum of the rabbit 'anti-human serum' when dropped into a clear solution of human serum causes a precipitate,—not with the serum from another animal. The principal difficulty in the test is to obtain from the rabbit an antihuman precipitating serum of the proper strength. To be thoroughly reliable and specific *the formation of the precipitate must begin in five minutes and be complete in thirty minutes*. Old blood stains respond as well as recent. It has been stated that the blood of mummies, 3,000–5,000 years old could be identified as human by the method.

Examining mosquitos which had been in contact with certain animals it was possible to determine with accuracy the species of the animal each mosquito had bitten and to prove absence of human blood.

The test was employed in the Clapham murder case. A human blood stain taken up with normal Saline and some anti-human Serum added causes a white cloudy ring,—not so the stains from animal blood. Specific sera injected into a rabbit form an equally specific anti-serum—in other words, human anti-serum, will infallibly detect human blood,—a horse anti-serum will detect horse's blood and so on.—*P.J. i./11,202*.

Indian experience with the test was that it is absolutely trustworthy,—the reaction is not effected by the decomposition of the blood, by heat, etc. Fowl's blood used instead of rabbit's. Failures with goat's and monkey's blood.—*B.M.J. i./11,1481*.

Recent description of the Technique of the precipitin test.—*Anal.*, '28, 5.

Hydatid Fluid may be used to give precipitin test as aid in diagnosis. Interaction between hydatid fluid and serum from hydatid patients has been obtained.

Hydatid disease. Complement-fixation as mode of diagnosis. Found to be of considerable value in the few cases available,—positive results are conclusive, negative difficult to interpret. Hitherto the method of diagnosis has been the verification of eosinophilia,—this is, however, characteristic of almost every form of vermiform parasite.—*L. ii./10,377*.

Blood in Urine.—To test for, heat the specimen with strong potash or soda. If present a colour described as bottle-green is produced, and earthy phosphates coloured brownish-red by blood are precipitated.

Ozonic Ether and Guaiacum Test for,—add a drop or two of Tincture of Guaiacum—Guaiacum Resin 1, in Alcohol (90%) *q.s.* to 10—to a small quantity of the urine, shake and 'layer' Ozonic Ether on to the mixture. A blue colour at once, or on standing, indicates presence of blood—Iodine in the urine also gives this colour (*e.g.* if patient has been treated with iodides). Further, pus gives it with Guaiacum Tincture alone, the colour disappearing on heating.

Modified Guaiacum Test using Sodium Perborate.

To about 5 Cc. of the liquid add 1 to 5 drops of fresh saturated Alcoholic Solution of Guaiacum Resin, then about 1 Gm. Sodium Perborate and about 10 Cc. of 30% Acetic Acid, shake the mixture once and pour Alcohol carefully into the tube to form a separate layer,—a blue or blue-green color at the junction in five minutes will be formed, or green if only a trace. The test is said to show 0.035 Gm of blood in a litre.

of water. The Guaiacum resin used must show a *brown*, not a greenish fractured surface.

In our laboratory we found this to indicate 0.02 Gm. of blood per litre, i.e., 1 in 50,000. It is about five times as delicate as the Ozonic Ether Test. A green colour should be disregarded as we found a blank test gives a green. Fresh Solution of Guaiacum had no advantage over seven months old Simple Tincture of Guaiacum.

Blood, Recognition of, in Stains.—Plunge the cloth into boiling water for a few minutes, place on slide and add few drops of Ammonium Sulphide. Examine microspectroscopically for absorption bands of hæmochromogen. May be increased by 10% Potassium Cyanide Solution. If on a weapon or piece of jewellery, moisten with Ammonium Sulphide and scrape off sufficient and examine as before.

Oxyhæmoglobin in solution with a little Sodium Chloride evaporated over Sulphuric Acid to syrup consistence. Mixed with fifteen times its volume of Glacial Acetic Acid and heated on a water bath several hours the mixture yields, on cooling, flat rhombic crystals of Hæmatin Hydrochloride with dark violet colour and lustre—this is one of the recognised tests for blood stains.

Blood Stains on Clothing, etc.—The Guaiacum Test is highly spoken of. The stain must give a red aqueous extract yielding no coloration to a straw-coloured solution of Guaiacum in alcohol 90% when applied by itself but a blue colouration within one second on further addition of Hydrogen Peroxide. Oxidisers and enzymes give a reaction with Guaiacum Solution alone. Blood does not.—Analyst, 1912; Y.B.P., 1913, 40.

Recognition of Blood Stains.—Chloral Solution to extract blood stains. The stain is moistened with Acetic Acid and then soaked in a 70 to 80 per cent. solution of Chloral Hydrate for one or several hours if necessary. To the solution add a few drops of the Reagent (Guaiacum, Barbaloin, or Benzidine), then add Hydrogen Peroxide 10 volume strength diluted with double volume of Alcohol and slightly acidified with Acetic Acid (carefully superposed). The presence of Pyridine greatly accelerates and intensifies the reactions.

Hæmochromogen Crystal Test for Blood.

Reagent—Takayama's Solution 2 (an improvement on an earlier solution '1,' used in 1912). Caustic Soda solution 10% 3 Cc., Pyridine 3 Cc., Saturated Grape Sugar solution 3 Cc., Distilled Water 7 Cc. The solution keeps for one to two months.

Two or three drops are added to a small piece of the suspected material on a slide and covered with a cover glass. Salmon-pink crystals of characteristic appearance usually appear within 6 minutes in the cold. By warming the slide until bubbles just appear the crystals are formed almost at once. In the many types of stains tested the Hæmochromogen crystals were readily obtained cold, whereas in some cases hæmin crystals were not obtained at all, or only with difficulty.—D. J. A. Kerr and V. H. Mason, B.M.J. i./26, 134.

Benzidine Test for Blood in Urine and Pathological Material.

Benzidine. *Syn.* *p*-Diamidodiphenyl.— $\text{NH}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{NH}_2=184.112$ Grey crystalline powder soluble 1 in 19 of 90% alcohol, insoluble in cold water. is used as blood test.

Benzidine Hydrochloride is insoluble in 90% Alcohol and in water.

Employ a 1% solution of the base in 90% alcohol or 1% solution in a mixture of equal parts Glacial Acetic Acid and water. Whichever is used the result is practically identical. There is merely a difference in the shade of blue produced in the presence of blood.

To apply the test add to 2 Cc. of the Benzidine solution about the same quantity of 20 volume Hydrogen Peroxide. Mix and add 2 Cc. of the liquid to be tested. A blue colour forms at once if blood is present. The density of the colour corresponds to the amount of blood. Always conduct a control with normal material alongside.

Alternatively, mix 2 Cc. of the specimen with a few drops Benzidine solution and layer carefully with ozonic ether. In this case a blue ring is formed.

By the above test we found that 1 of blood in 1000 of liquid is easily detected.—indeed, we have been able to detect a far smaller amount—even 1 in 100,000.

Diastases, Zymases, Fruit Juices give similar reaction. A positive reaction does not prove blood, but the negative proves its absence.

The test is less specific if material has been strongly heated.—B.C.A., Sept. '28, 1046.

Tablets of Benzidine 0.1 Gm. and Sodium Perborate 0.1 Gm. Just before use dissolve a Tablet in 10 Cc. Glacial Acetic Acid. If a suspected spot on an article of clothing, etc., is to be examined, it is moistened with a drop of Normal Saline and well rubbed with a glass rod. The drop is then absorbed in a small piece of absorbent cotton wool and the spot at once treated with a few drops of the Reagent. In presence of blood a blue color is seen.

Weber's Guaiacum Test. Make Ether extract as above and add 8 to 10 drops Guaiacum Tincture and Hydrogen Peroxide. Definite blue colour in 2 minutes. For albumin add equal volume of saturated solution of Ammonium Sulphate, filter, acidify and warm.—R. Coope, L. ii./20, 291.

Benzidine Test is very sensitive and simple.—A. Abrahams, L. ii./20, 420.

Kastle-Meyer Test for Detection of Blood.

Mayer's Phenolphthalin Reagent, as described under *Fæces* is used.

The technique consists in adding 10 to 20 drops of the reagent to the suspected blood-stained surface, then adding a few drops of fresh 20 Vol. Hydrogen Peroxide. If blood is present, a deep permanganate colour develops almost immediately. The Test is of value for detecting hæmoglobin medico-legally.—J. Glaister, B.M.J. i./26, 650.

Doubt as to reliability of the test. Aspirin and other drugs, also a red meat diet, may confuse. Cannot be accepted in a court of law.—D. Kerr, B.M.J. i./26, 721.

Thymolphthalein as Blood Test.

Dissolve Thymolphthalein 1 in water 100 and add Potassium Hydroxide 25 and Zinc Powder 10. Boil until colorless, filter hot and make up to original volume. Keep Zinc filings in the solution to prevent oxidation.

To use the test, rub down a small portion of the *fæces* (e.g. size of a bean) with 5 to 10 Cc. of Alcohol and 20 drops of Glacial Acetic Acid. 25 to 30 drops of the Extract are filtered off and 20 drops of the reagent added mixed with 15 drops of Hydrogen Peroxide. On shaking a greyish-blue opaque ppt. forms turning blue on standing if blood is present.—Y.B.P. 1919, p. 46.

See also *Fæces*, p. 412.

Choline.—Halliburton and Rosenheim's Test for in the Blood and Cerebro-spinal Fluid.—Dark brown crystals (Choline Periodide) resembling hæmin appear on adding a strong solution of Iodine in Potassium Iodide to Choline-platino-chloride crystals. To prepare the Platino Chloride of Choline is, however, not essential, as the test can be applied direct to the Alcoholic Extract of the fluid.

The MARCHI REACTION for showing nerve degeneration consists in the fact that the fatty acid (decomposition product of Lecithin) stains black with Osmic Acid even in the presence of Chromic Salts while Lecithin does not.

The products of degenerative nerve disease, notably Choline, can be detected in the blood and cerebro-spinal fluid. *Further on Choline Vol. I., p. 7.*

Hæmoglobin Estimation.

Gowers' apparatus consists of two tubes, flattened or round, one closed containing picro-carmin solution—the standard equal to the colour of a dilution of average normal blood one hundred times (20 cmm. in 2 Cc.) and the other, graduated in 100 degrees = 2 Cc. for the dilution of the sample of blood with distilled water. The outfit further includes a pipette, pricker, india-rubber stand, &c.

The lobe of the ear or the finger is pricked and 20 cmm. of blood are drawn up into the pipette, injected into the graduated tube, which should at the time contain a few drops of water to prevent possible coagulation and facilitate mixture. Water is then added sufficient to produce a tint the same as the standard, the two being frequently compared during the process. The degrees of dilution needed indicate the percentage amount of hæmoglobin. For example, 20 cmm. of blood from an anæmic patient giving the standard tint at 30 degrees of dilution would contain only 30% of the normal quantity of hæmoglobin.

Haldane's Modification of Gower's Hæmoglobinometer is also employed. The standard tint tube is a 1% solution of blood containing the average percentage of hæmoglobin found in the blood of healthy adult men, and having an oxygen capacity of 18.5% as determined by the ferricyanide method. *The solution is saturated with carbon monoxide*, and hermetically sealed. It is both definite and permanent. The graduated tube holds 2 Cc. when filled so that the inside is completely wetted and the liquid stands at the mark 100 after half a minute has been allowed for the upper part to drain. The tube is graduated in percentages of 2 Cc. A cap for attachment to a gas-burner serves to deliver gas for saturating the diluted blood with CO.

The advantages of the modifications are: (1) that the standard solution is a definite one, so that an instrument can be verified at any time by making a determination with ox-blood of which the oxygen capacity has been determined by the ferricyanide method; (2) that the standard solution is permanent; (3) that the apparatus can be used with equal correctness by daylight and artificial light.

As coal-gas is not always available in examining the blood of patients the instrument can always be supplied with an additional standard tube containing picro-carmin solution, as in the original Gowers' Hæmoglobinometer. The solution is standardised to correspond with blood of 18.5% oxygen capacity, but is liable to slow alteration on keeping. Its value in terms of the sealed tube of blood solution should therefore be occasionally ascertained by determining the hæmoglobin in blood from the same person, first by the picro-carmin standard and afterwards by the sealed blood standard. The difference gives the percentage correction needed for the picro-carmin standard. The picro-carmin standard should not be exposed unnecessarily to light.

Sahli's Hæmometer and **Dare's Hæmoglobinometer** are also used.

The **Dare Hæmoglobinometer** permits the colour of a thin film of undiluted blood to be compared with a graduated colour scale under standard lighting conditions, and by means of a scale the hæmoglobin count can be directly read, the entire operation occupying about 2 minutes.

Tallquist's Hæmoglobin Scale consists of a scale of colours with strips of blotting paper to suck up the blood for examination. The tint thus produced is compared by direct light with the scale which indicates 10, 20, 30, &c., up to 100. This refers to amount of hæmoglobin—100 being normal.

Estimation of Corpuscles.

One cubic millimetre contains normally about 5,000,000 to 6,000,000 red corpuscles in man, and about 4,500,000 in woman. The average number of white corpuscles per cubic millimeter is about 7,000 to 8,000 in adults, and 10,000 in children.

The hæmacytometer chiefly used is the Thoma-Zeiss or Thoma-Hawksley.

This consists of a micrometer slide divided into 16 squares, each again divided into 16 smaller squares. It has two pipettes, one for diluting the blood 1 to 100 for counting the red corpuscles, the other is intended for estimation of the leucocytes, and dilutes the blood 10 times. The number of red corpuscles seen in 4, 6, or if greater accuracy is required, 16 (larger) squares, i.e., in 64, 96 or 256 smaller squares, is counted.

Estimation of Red Corpuscles.—To ascertain the number in 1 cmm. of blood, knowing the volume of the cube standing on each small square to be $\frac{1}{1000}$ cmm., multiply the total number of red corpuscles counted by 4,000 times the number of times of dilution of the blood and divide the result by the number of small squares in which red corpuscles have been counted. It is always desirable to have an assistant to note the numbers observed, and to count the corpuscles touching and overlapping the two adjacent boundary lines on the left upper corners of the squares, but those on or overlapping the other two sides are excluded to compensate.

The normal dilution is 1 to 200; in polyemia 1 to 400; and in excessive anemia 1 to 100 may be used. 5 or 6 corpuscles per square are a convenient number for counting.

The Thoma-Zeiss cell is $\frac{1}{16}$ mm. deep and each side of a small square is $\frac{1}{16}$ mm., hence the above figure $\frac{1}{4000}$ cmm. as the volume of a small square.

The **Burker Hawksley Counting Chamber** consists of 2 cells, and thus permits of 2 counts being taken at once, and any errors from atmospheric

pressure are obviated by a portion of the cell platform projecting beyond the edge of the cover glass.—A. Cecil Alport, L. ii./22,756.

Gowers' Hæmacytometer Solution is also used for diluting. Sodium Sulphate 104 grains, Acetic Acid 1 drachm, Distilled Water 4 ounces. Filter.

Hayem's Solution is also employed. Sodium Chloride 2, Sodium Sulphate 5, Mercuric Perchloride 0·5, Water 200.

Toison's Solution is also employed. It stains the leucocytes, see below.

Wright's Diluting Fluid for counting red corpuscles. Sodium Chloride 1, Mercuric Chloride 0·2, Distilled Water to 100.

Edington's Hæmacytometer Solution.—Sodium Citrate (neutral-7·5 Gm. Formalin (40% Commercial), 2·0 Cc. Dahlia (Methyl Violet), 0·03 Gm. Chloroform 5 drops, Distilled Water 250 Cc. Mix the stain with the water, then add the Sodium Citrate and the Formalin. Has the advantage that in less than 1 minute, all the corpuscles are deposited on the slide and in focus. The refractive index of the corpuscles is well maintained.

The '**Color Index**' is the index of corpuscular richness. It is obtained by dividing the percentage of Hæmoglobin by the percentage of Red Corpuscles. With the normal of Red Corpuscles as 5,000,000 and the Hæmoglobin at 100 the index is $\frac{100}{5000000} = 1$. In a case of Red Corpuscles 4,000,000 (= 80% of normal) and Hæmoglobin 40%, the index would be $\frac{40}{4000000} = 0·5$. Consult Emery's work for importance of this index in differentiating chlorosis, pernicious anæmia and in other types of anæmia.

Estimation of Leucocytes may be conducted in a similar manner, by the **Thoma-Zeiss** instrument, but in this case it is desirable to stain them before counting by using Gowers' diluting fluid, with an appreciable addition of Löffler's Methylene Blue, or by **Toison's Solution** (Dissolve Methyl Violet 5 B. 0·025 Gm. in a mixture of Glycerin 30 Cc. and Water 80 Cc. Dissolve separately Sodium Sulphate 8 Gm. with Sodium Chloride 1 Gm. in Water 80 Cc. Mix and filter). Leucocytes stained violet, red corpuscles greenish. For accuracy count as many squares as possible.

A further formula for the staining fluid is Formalin 1·5, Sodium Chloride 0·5, Sodium Sulphate 2·5 Methyl Violet 0·01, Water 100.

Another method is to use an aqueous $\frac{1}{2}$ % acetic acid solution as diluent, in this the red corpuscles become invisible while the leucocytes remain visible (Thoma-Zeiss).

In **LEUCOCYTOSIS** the number of white corpuscles may be increased from the normal 7,000 or 8,000 up to 12,000, or even to as many as 1,000,000 per cubic mm.

Leucocytes in Normal Blood.

- | | |
|--------------------|--|
| (Regular Nuclei). | (1). Lymphocytes, small
large } 25% (L.) |
| | (In childhood more numerous,—up to 60%). |
| | (2). Hyaline (large Mononuclear Cells) 1 to 2% (H.) |
| | (3). Transitional Cells 1 to 2% (T.). |
| (Irregular Nuclei) | (4). Polymorphonuclear neutrophils 70 to 80% (P.).
(In childhood only 30 to 40%). |
| | (5). Oxyphile cells (Eosinophile Leucocytes) 3 to 5% (E.). |
| | (6). Basophile Cells (Mast Cells) 0·5% (B.). |

(Often not found in persons in robust health.)

The cells comprised in Nos. 1 to 3 are sometimes called the non-granular whilst those in 4 to 6 are called the granular leucocytes, i.e., they contain granules in their protoplasm. The initial letters are commonly used for counting purposes.

Strong's Method. The stain is composed of Methyl Violet 0·012 Gm., Sodium Chloride 0·75 Gm., Formalin Solution 1·5 Cc. Distilled Water 100·0 Cc.

A method of blood-counting producing permanent preparations which may be used subsequently. Eliminates ruled counting chamber and error due to variations in the depths of the cells.

Leucocytes, a Simple Method of Counting. To stain, a 3% sodium chloride solution deeply coloured with Gentian Violet is sufficient. It is simpler to count whole microscopic fields of known area rather than squares. Employing the 1 in 20 pipette, count whole microscopic field, not the squares, move the draw-tube of microscope into such position that $7\frac{1}{2}$ squares in diameter

(Thoma-Zeiss scale) are in view. The cubic contents of this = $\frac{1}{16}$ Cmm. Make a mark on the draw-tube—to be used for all occasions. Count twenty fields with above dilution, and add two cyphers to the number so obtained.

A further simple method of counting.

Draw up measured quantity of blood with capillary tube and pipette, and in the same manner ten times as much water, mix on watch glass. Drops (all the same size of the mixture are arranged on a slide (s.g.) in line. Dry slowly in the sun or before a fire, then gently agitate in a dish of water until all pigment is washed off. Examined under the microscope each spot will be seen to consist of a faint amount of debris with dark conspicuous leucocytes. They may be stained with Methylene Blue if preferred. Count the cells in several fields, using $\frac{1}{4}$ in. objective, a stiff paper obturator (pierced with ranks of 20 or more holes made by a large needle—each, on an average with normal blood, to show 2 or 3 leucocytes per hole) is fitted in the eyepiece. If 10 films be searched thus, a good average will be obtained. Two to four fields, each from a different film, is sufficient to count as a rule. The average number per field for normal persons is noted—i.e., 8,000 per cmm. A simple comparison indicates degree of leucocytosis.

Total and Differential Leucocyte Count conducted simultaneously.

Diluent employed is a mixture of Wright's Modification of Leishman's Stain 4, Acetone 3, Methyl Alcohol 1, Water 12. This is used freshly made up and filtered in any dilution from 1 in 200 to 1 in 10. The white cells stain as in a film, whilst the red are colourless. A dilution 1 in 100 gives about 80 cells on the large square of a Thoma-Zappert Slide which is enough for the total count, whilst 300 elsewhere can be found for the differential. In marked leucopenia, a 1 in 10 dilution gives as many cells as required in a few minutes. In many cases a glance gives the result, e.g., a marked eosinophilia, or excess of lymphocytes, large mononuclears or polymorphic cells. The stain is mixed with the blood in a small tube, e.g. a Haidane Haemoglobinometer tube cut down to the 120 mark. With this, 24 divisions of water and the rest in proportion are sufficient for a 1 in 100 pipette if it can reach to the bottom.—L. i./12,20.

Note.—All tinting solutions should be freshly prepared.

The method was found unsatisfactory in hot weather. The following was preferable.—make a $\frac{1}{2}$ saturated solution of Wright's Stain in Methyl Alcohol by adding 5 Cc. of Methyl Alcohol to 10 Cc. of Saturated Solution. Add 1 part of this to 3 of Saline, 0.1% strength. Stains well without precipitating on the slide.—L. ii./12,1179.

Cases illustrating the value of an examination of the blood—by blood counts, estimation of hæmoglobin and Serum Tests.—E.H.Shaw, L.ii./12,286.

Value of blood examinations in diagnosis—tables showing blood changes in various diseases.—S. Wyard, Clin. Jl. April 25/23,195.

Volume of Blood.—Method of estimating. The principle employed was to inject into the blood stream a known amount of hæmoglobin, and then determine degree of resulting hæmoglobinæmia.—B.M.J. i./09,1357.

In **PERNICIOUS ANÆMIA** the red corpuscles, instead of 5,000,000 or more per cmm. are only 2,000,000 or even as low as 1,000,000. Hæmoglobin is also reduced, but not to an equal extent.

Hæmolytic Action of Urine in cases of pernicious anæmia. Incubation at 37° C. of the blood emulsion with the specimen of the urine effects laking, but this does not occur with the urine in health. It also occurs in other disturbances of metabolism, and is not diagnostic or prognostic of pernicious anæmia. Sodium Bicarbonate influences the reaction *in vitro* and possibly when given to patients *per os*.—C. S. Mackie, B.M.J. ii./15,596.

Arneth Index.—The number of lobes of the nuclei in neutrophile leucocytes although constant in health is altered in infectious diseases. (Arneth Deut. Med. Woch. 1904, i. 54), divided neutrophile leucocytes into five classes according to the number of nuclei contained, and further divided these five classes into three, four or more subclasses dependent on the shape of the nuclei. Class I. and II. are the most important—those comprising one or two sub-divisions of the nucleus. The Index is the sum of these two found in counting 100 such cells. There is a well marked increase of Classes I. and II. in infectious diseases which he called a shift to the left. In pulmonary tuberculosis (1) the shift to the left is in proportion to the extent of the disease;

(2) as the patient improves the index moves more to the normal; (3) unless the index is normal no case can be regarded as really cured. Experimental work in part confirmation. Bibliography.—H. A. Treadgold, L. i./20,699,920. A count with more than 40 in I. and II. is abnormal.—W. E. Cooke, L. ii./28,1040.

Blood Staining.

To make films, prick patient's finger, press, let first drop of blood fall away, place the next drop (small) on the centre of a *really clean* $\frac{7}{8}$ in. square cover slip. Superpose another and pull off so that the film is thin and even—not 'ridges' and 'valleys' and dry in the air. No fixing is necessary, the Methyl Alcohol in the stain (Leishman, etc.) does this.

Jenner's Stain is used. It may be prepared by mixing freshly 100 Cc. 0.5% Solution of Medicinal Methylene Blue in Absolute Methylic Alcohol with 125 Cc. of a 0.5 Solution of Eosin (water soluble yellow shade). Filter. A similar stain is produced by dissolving Eosin-Blue in Methyl Alcohol.—*cf.* Leishman's Stain.

Method of use.—Add $\frac{1}{5}$ volume of Distilled Water to the Stain when on the film (*e.g.* 1 drop to 5 drops), and rock gently. Stain for five minutes, then wash in distilled water until pink tint replaces greenish colour. Remove excess of water by filter paper and dry in the air without heating.

Should be kept in stoppered bottles well closed, and is best recently prepared. The Methylene Blue and Eosin are said to combine, forming a chemical compound. In staining it is important to cover with a watch glass to prevent evaporation of the Methyl Alcohol.

Jenner's Stain is, we found, improved by using *Polychrome Methylene Blue* in place of ordinary Methylene Blue. The 'polychromatising' we effected by adding finely powdered crystalline Sodium Carbonate to the Methylene Blue Solution in the proportion of 1 Gm. of Sodium Carbonate to each 2 Gm. of Methylene Blue. This gave a stain in which blue elements overstained by using Jenner's directions, but by using Wright's method (covering film with a few drops of the Stain, allowing to stand 10 seconds, and diluting with two volumes of water) the resulting film was good.

We also found that the proportion of the Eosin Solution may be increased, *e.g.*, Eosin Solution 2 and (*Polychrome*) Methylene Blue Solution 1, gave good result.

Romanowsky's Stain, Leishman's Modification.—There are various modes of making and supplying this stain. The following as suggested by Leishman gives the best results (the fixing and staining is done in one process so that fixing by heat is unnecessary):—

This is a solution in pure Methyl Alcohol of an Eosin-Methylene-Blue-precipitation-compound, 0.15 grammes of the compound being dissolved in 100 Cc. of Methyl Alcohol. The solution thus formed is a clear dark blue liquid showing a green iridescence by reflected light. The Stain is used by preparing films of blood in the usual way on clean cover glasses, and allowing to dry in the air. The films should be as thin as possible. Three or four drops of the Stain are dropped on to the film and the cover glass is rotated, no attempt being made to check evaporation as in the case of Jenner's Stain. After about half a minute six or eight drops of water are added, and allowed to mix by rotating with the Stain, and staining is allowed to proceed for five minutes, in certain cases ten minutes may be necessary. The film is now washed with distilled water, and a few drops of the water are allowed to remain on it for one minute. It is finally dried without heating and examined with an oil immersion lens.

(Note, the strength of the Stain may in some cases have to be increased somewhat, the volume of water added in staining may require modifying,—e.g., to the same volume as that of the stain or less.)

Note.—Leishman in his original paper (B.M.J. ii./oi,757) directs Methylene Blue to Eosin* in proportion 10 to 1 to make the precipitation compound. Reckoning water-soluble Eosin as of formula $C_{20}H_6O_5Br_4Na_2$. = 691.706 or with $6H_2O$ about 800, it may be pointed out that this does not appear to have any relationship with Methylene Blue which has composition $C_{12}H_8N_3S(CH_3)_4Cl$ approx.

1. Mol. Eosin of above formula should be equivalent 2 Mols. Methylene Blue = $2 \times 320 = 640$. In some experiments which we conducted using ordinary Commercial Methylene Blue cryst. $6.4 \text{ Gm.} (= \frac{2 \text{ Mol. Wts.}}{1 \text{ Mol. Wt.}} \frac{100}{100})$ and Eosin (water soluble, yellow shade) $8.0 \text{ Gm.} (= \frac{100}{100})$ in 1% solutions each; mixing

as directed, adding $2.8 \text{ Gm.} (= \frac{100}{100})$ of Sodium Carbonate cryst. and

boiling half an hour, collecting the precipitate and washing until runnings were of pale blue color, we obtained a *better yield* than by Leishman's Method. The precipitate, as above dissolved in the requisite proportion (0.15%) in Methylic Alcohol stained blood films satisfactorily. But even on these lines no chemical formula can be devised to show the reaction. The Stain appears to be based rather on experimental finding.

The following results are obtained:—

RED BLOOD CORPUSCLES are stained pink.

POLYMORPHONUCLEAR LEUCOCTES red. Nuclear network blue. Extra nuclear protoplasm colourless. Fine eosinophile granules red.

MONONUCLEARS or HYALINE or LARGE LYMPHOCYTES.—Nuclei pale blue. Extra-nuclear protoplasm blue, occasionally showing red granules.

TRANSITIONAL.—As with large mononuclears, except nucleus is reniform.

SMALL LYMPHOCYTES as mononuclears, except nuclei deeper stained.

COARSELY GRANULAR EOSINOPHILES.—Nucleus blue but not so deep. Granules pink.

BASOPHILES.—Granules deep-stained purple black. Nucleus red but usually somewhat masked by granules over-laying it.

NUCLEATED RED CELLS.—Nucleus almost black with sharp outline. Extra-nuclear portion grey.

MYELOCYTES stain pale red nuclei pale blue.

BLOOD PLATES deep red with spiky margins, often with pale blue peripheral zone.

BACILLI and MICROCOCCI blue.

MALARIAL PARASITES.—Body stains blue and its chromatin deep red. *Vide* also Malarial Parasites, this Vol.

A small proportion of Glycerin, it is stated, intensifies the Leishman and allied stains and shortens exposure.

LEISHMAN'S STAIN (WRIGHT'S MODIFICATION).—Add Methylene Blue 1 Gm. to 100 Cc. of 0.5% Sodium Bicarbonate Solution. Sterilise in a flask in a steam steriliser for one hour. Place in a large dish and add while sterilising,

*Eosins and Erythrosins.

The name Eosin is used for the Sodium or Potassium salt of tetra-brom-fluorescein, while the Alkali salt of dibrom-fluorescein is Eosin-Orange.

Eosin may be made from Fluorescein by brominating in presence of alcohol or water, in the former case with a little oxidising agent added.

Erythrosins are the corresponding Iodine compounds. The di-iodo body is known as Erythrosin 'G' or Pyrosin, the tri-iodo as Erythrosin 'A' and the tetra-iodo as Erythrosin 'B,' Iodo-eosin or Tetra-iodo-eosin. The latter two names are incorrect, Eosins being Bromine derivatives as stated. Commercial samples (German) may contain Sodium Sulphate, Sodium Chloride and other halides.—T. T. Cocking and co-workers, B.P. Conf., 1919.

Erythrosin, 0.2% solution injected has been used in conjunction with the Finsen lamp.

1 in 1,000 Eosin Solution (yellowish, soluble in water) until the mixture changes to purple and shows yellowish scum on the surface. About 500 Cc. of the Eosin Solution will be required. Collect precipitate formed, and dry in an incubator without washing. When thoroughly dry dissolve 0·3 Gm. of the powder in 100 Cc. pure Methylic Alcohol. Filter this saturated solution and add to the filtrate further 25% of Methyl Alcohol, i.e., to 80 Cc. add 20 Cc. It is now ready for use.

Method of use.—Pour stain on to film and stain one minute. Add water drop by drop until greenish scum forms on surface (for $\frac{7}{8}$ inch cover glass 6 to 8 drops required), stain with this further two minutes, wash in distilled water and soak in same 2 minutes or more, until the thinner parts of film appear yellowish pink, dry with filter paper (no heat) and mount in Xylol Balsam.

Normal Erythrocytes appear yellow or pink. In cells deficient in hæmoglobin the colour is from a pale pink with large central clear space to dirty yellow. Polychromatophilic cells bluish. Granular degeneration or basophilic degeneration shows well as small bluish dots in a pink cytoplasm. Normo-blasts have a pink cytoplasm and blue nucleus (in some the cytoplasm is yellowish, purplish, or bluish). Megaloblasts show blue nucleus and yellowish or bluish cytoplasm.

The various solutions of Eosinote of Blue lose their differential staining power particularly with regard to the granules, after keeping a few weeks (especially in hot weather). Jenner's and Leishman's Stains may be "reactivated." by adding a very small quantity of the original powder.

***Endolytic Tubes of Leishman's Stain, Methylene Blue and Carbol-Fuchsin** are prepared and are convenient as they keep indefinitely.—J. C. Matthews, L. ii./22,260.

Wingrave's Blood Stain.

Two stock solutions are used :—

I. Methylene Blue saturated solution in 90% (Rectified) Alcohol

II. Eosin (Water Soluble) saturated aqueous solution.

Directions.—Well mix 4 Cc. (about 60 drops) of No. I. with 1 drop of No. II. Flood the film in a Petri dish for three minutes, then add 2 or 3 drops of Distilled Water and stain for 3 to 5 minutes, oscillating constantly, wash well in Distilled Water, then dip into a developer composed of tap water 100 Cc., Glacial Acetic Acid 2 drops, several times quickly and dry with best filter paper. Mop off excess and examine direct. Should Eosin be in excess nuclei will be pale, therefore add more blue. Filtering is not necessary.

May Grünwald's Stain is a Methylene Blue—Eosin Mixture similar to Jenner's Stain, which was used for typhoid diagnosis.

Blood films well stained by May Grünwald's Stain in conjunction with Giemsa's stain. Brings out the azure granules excellently. Pour on the May Grünwald Stain and allow to act 3 minutes then add equal quantity of water and stain 1 minute. Pour off stain and without washing add Giemsa's stain diluted to about 15 drops in 10 Cc. of water. Stain 15 minutes and dry.—H. M. Cade, B.M.J. i./22,939.

A stain comparable with the Romanowsky stains and of remarkable intensity, it is stated, may be made as follows: Medicinal Methylene Blue 1·00 Gm. and Eosin 0·40 Gm. are dissolved in a flask in Methyl Alcohol 40 Cc. Absolute Alcohol 80 Cc. is added, then Glycerin 30 Cc., drop by drop, and then Ammoniacal Silver Nitrate solution, 3 Cc. Boil the mixture 3 or 4 minutes in water bath and shake well. Filter when cool. Place 15 drops on the unfixed film, prevent evaporation, and leave for 1 or 2 minutes to fix. Add 15 Cc. distilled water to the dish containing the slide, mix and stain for 5, 10 or 15 minutes. Wash.—Motais, T.D.B., Vol. 17, 1921,109.

Gauducheau's Stain *v. chapter on Malaria.*

Knyvett Gordon's Stain.

The following simple stain gives results indistinguishable from the panoptic method, i.e., Jenner's followed by Giemsa's stain, which is essential in the diagnosis of pernicious anæmia: Eosin-methylene Blue 0·02 Gm., Eosin-methylene Violet 0·02 Gm., Methyl Alcohol 25 Cc. Stain for one minute, then add equal volume of Distilled Water, leaving diluted stain for 3 minutes. Follow with water for 2 minutes, dry, and mount.—A. Knyvett Gordon, L.i./25,127.

Ehrlich-Blondi Stain *Syn.* **EHRlich-BIONDI-HEIDENHAIN MIXTURE, EHRlich's TRIPLE STAIN**

This nuclear stain is prepared by dissolving separately Methyl Green 1 Gm. in water 200 Cc., Acid Fuchsin 1 Gm. in water 80 Cc., Orange G 4 Gm. in water 400 Cc., and mixing afterwards. The stain is then ready for use; it is *not* to be further diluted. Sections should be allowed to stain from 6 to 24 hours. Dehydration is effected with Alcohol, and the sections are cleared with Xylol and mounted in Xylol Balsam. Slides stained 2 to 10 minutes by this process show:—

ERYTHROCYTES, orange. **NEUTROPHILE POLYMORPHONUCLEAR GRANULES**, violet.

NEUTROPHILE MYELOCYTES, violet. **ACIDOPHILE GRANULES OF THE POLYMORPHONUCLEAR CELLS**, brick red. **BASOPHILES**, not stained. **LYMPHO CYTES**, Nuclei, pale greenish blue. **CYTOPLASM**, faint pink or grey. In disease the nuclei of the erythroblasts are greenish black. This triple stain should be distinguished from—

Triacid Stain.

Orange G. saturated aqueous solution 12, Acid Fuchsin saturated aqueous solution 8, Methyl Green saturated aqueous solution 10, water 30, absolute Alcohol 18, Glycerin 5.

The former of these two stains is the more used. The Triacid Stain appears to be more powerful, but is perhaps less delicate.

Ehrlich's Hæmatoxylin Solution.

Dissolve Hæmatoxylin 1.5 gm. in Alcohol Absolute 100 Cc., and mix the solution with a 100 Cc. of saturated solution of Ammonia Alum in water to which has been added Glacial Acetic Acid 5 Cc. and Glycerin 100 Cc.

Grenacher's Alum Carmine. Carmine 1, Alum 5, water 100. A small amount of Phenol may be added to preserve. For nuclei and muscle staining.

Grenacher's Hæmatoxylin Solution.

Dissolve Ammonia Alum 45 in water 430. Dissolve separately Hæmatoxylin 2.4 in Absolute Alcohol 12. Mix and allow to stand for 14 days. Filter and add Glycerin 66 and Alcohol 90% 75 Cc.

Delafield's Hæmatoxylin Solution is similar.

The presence of Methyl Alcohol in addition to Ethyl Alcohol is unnecessary in Delafield's Hæmatoxylin Solution. A series of sections (showing mitosis) stained with batches of the stain made with (1) the usual mixture and (2) with Ethyl Alcohol, alone showed no difference in depth of stain and sharpness of definition in the chromosomes.—H. Garnett, P.J. i./18,127.

Borax Carmine. This solution is prepared by boiling Alcohol 70% with Carmine and Borax in excess, and filtering after cooling.

Mayer's Stains: **Carmalum**—Carmine 2, Alum 5, boil 1 hour with water 100, filter. **Hæmalum**.—Hæmatein [$C_{16}H_{12}O_8=300.096$]. 1. dissolved in alcohol Absolute 50. Mix this solution with one of Alum, 50. in water 1,000. **Acid Hæmalum** consists of the above, with 2% Acetic Acid added. **Hæmatoxylin or Kleinenberg's Hæmatoxylin Solution.** To a saturated 70% Alcohol Solution of Alum and Calcium Chloride, diluted with 6 times the amount of Alcohol of the same strength, is added Alcoholic Solution of Hæmatoxylin, until the characteristic violet colour is produced. **Paracarmine.**—Carminic Acid 1, Aluminium Chloride 0.5, Calcium Chloride 4 in Alcohol 70% 100. **Picrocarmine.**—Saturated Picric Acid solution is added to a solution of Carmine 8 Gm., in 100 Cc. of Ammonia until a precipitate commences to form.

Perenyi's Solution (Hardening Reagent).—Dissolve Chromic acid 0.15 Gm. in Water 30 Cc. and add Alcohol 30 Cc. and Nitric Acid (10%) 40 Cc. Employed for fixing plant and animal preparations.

A combined vital and non-vital method of staining corpuscles.—A. C Alport, L. ii./28,170.

Blood platelets in anæmias and acute diseases. Romanowsky Staining Methods best of the methods used. Diminution in pernicious anæmia, lymphatic leukæmia, purpura hæmorrhagica; increase in lymphadenoma and myelogenous leukæmia.—G. J. Crawford, L. ii./24,595.

Blood plate counts in pulmonary tuberculosis (normally the average was found to be 300,000 per c.mm.). Blood plates are generally present in excessive numbers in active pulmonary tuberculosis; the more serious the clinical

condition, the greater the degree of thrombocytosis. The number of red corpuscles is evidently of no value in prognosis.—R. G. Bannerman, L. ii./24,593. Technique *ibid*, 1154.

ACTION OF CERTAIN COMPOUNDS ON BLOOD PLATELETS AND LEUCOCYTES, when injected intravenously in rabbits :

	<i>Blood Platelets.</i>	<i>Leucocytes.</i>
Calcium Chloride.	Transient reduction.	Increased.
Sodium Citrate.	" "	Considerable decrease.
Physiol. Salt Solution.	Not affected.	Not affected.
Epinephrin.	Increased.	Unchanged or increased.
Histamine.	Increased.	
Nicotine.	Decreased.	
Acetylcholin.	Increased.	Not affected.
Pilocarpine (toxic doses).	Not affected.	Slightly increased.
Atropine.	Marked diminution.	Increased.

—Comptes Rend., per Jl. A.M.A. ii./25,856.

Calcium Salts in Blood, Estimation of, v. pp. 404 and 405.

Sugar in Blood v. Glucose, this chapter.

Blood Pressure is determined by some form of the **Riva Rocci Sphygmomanometer**, *e.g.*, that of **C. J. Martin**, or the **Beaumanometer**.

Directions are supplied with the instruments.

Viscosity of the Blood is determined by the aid of the **Viscosimeter (Du Pre Denning and Watson)**.

Coagulation Time of the Blood.

Brodie Russell Boggs' Coagulometer consists of an air chamber, into which a fine stream of air can be tangentially directed on to the edge of a hanging drop of blood, very light blowing being effected at 30 second intervals. The period which elapses from the exit of the blood from the vessel until coagulation has occurred is measured by the coagulometer and the aid of a microscope with low power objective. Records between 7 or 8 minutes are stated to be normal.

For **Sir A. E. Wright's and other Blood Coagulation Tubes** for measuring the coagulability of the blood see Edn. XVIII, Vol. II, p. 398.

There is a lessened coagulability in hæmophilia.

Reaction of the Blood, Determination of.

This method depends on the appearance of a precipitate when a definite amount of Acid is added to a definite amount of diluted blood. A series of small tubes are prepared containing quantities of $\frac{N}{1000}$ Sulphuric Acid rising by 0.1 Cc. from 0.0 to 1.2 Cc., the volume in each case being made up to 2 Cc. with Distilled Water. A drop (0.02 Cc.) of blood is then added to each tube, the contents well mixed, and the tube placed in a water-bath at 45° for one hour. With average human blood the tubes containing the smaller amounts of Acid show a slight opalescence, but a coarse, flocculent precipitate makes its appearance when the tubes containing 0.7—0.9 Cc. of Acid are reached. The appearance of this precipitate is considered to indicate the neutralisation point. The reaction is given equally well by fresh defibrinated, oxalated or citrated blood and by red corpuscles washed many times with salt solution. It is not given by citrated or oxalated plasma, by serum or by a solution of fibrin. It is supposed that the precipitate consists of the nucleo-protein of red cells.—J.C.S.A. ii./10,317 ex Arthur E. Boycott and R. A. Chisholm (Bio-Chem. Jl., 1910, 5, 23-31.)

F. Gowland Hopkins deals with the modern views on the Chemical Reaction of the blood and changes which occur. —L. i./24,1589.

Reactivity of the Blood in relation to cardiac breathlessness, surgical shock, etc. The 'strip' of variation in acidity or alkalinity of the plasma of the blood within which life is possible is a very narrow one, and it suffices to render the medium within which living cells are situated acid or alkaline to the feeble limit of one-thousandth, normal, or less, in order to destroy

life. Blood plasma is capable of being able to neutralise large amounts of either acid or alkali without itself being or becoming markedly acid or alkaline. A consideration of the variations in the property of balanced alkalinity and acidity (HYDROGEN ION CONCENTRATION).—Benjamin Moore, B.M.J.ii./18,251 cf. Prof. Bayliss, *ibid.* 78.

Hydrogen-ion Concentration of the Blood.

The reaction of the blood serum varies approximately between pH7 and pH8, the neutral point, pH7, being reached only in severe uncompensated acidosis and a reaction of pH8 being attained perhaps only after administration of alkalis.

The symbol p in pH means that power to which 10 must be raised to give the concentration in grammes of hydrogen-ion per litre of the fluid in question. Since it is always negative for solutions weaker than $N/1$ acid the $-$ sign is omitted. By a further convention H in pH stands for the Hydrogen-ion and not the element, though usually the ion is designated H^+ or more simply H° .—C. A. Lovatt Evans, *L. ii.*/21,867.

A series of Standard Solutions are required of known " pH " to be used in conjunction with a delicate indicator which will show easily recognised changes in colour due to Hydrogen-ion concentrations approximating that of the solution tested.

The method has been used by Henderson and by Walpole on the urine, but in the case of blood, coloring matter and proteins must be excluded by dialysing.

Collodion Sacs are employed. Blood dropped into these and dialysed for five minutes is free from interfering bodies but contains salts which are responsive to **Phenolsulphonephthalein**—an indicator showing differences in tint between pH 6.4 and 8.4.

The following solutions are first prepared :—

A. **$N/15$ Acid Potassium Phosphate (KH_2PO_4) Solution.** (9.078 Gm. per litre of fresh Distilled Water).

B. **$N/15$ Sodium Phosphate Solution** containing 11.876 Gm. per litre of $Na_2HPO_4 \cdot 2H_2O$ or the equivalent of the salt with $12H_2O$.

Mix solutions A. and B. as follows :—

pH	6.4	6.6	6.8	7.0	7.1	7.2	7.3	7.4	7.5	7.6	7.7	7.8	8.0	8.2	8.4
A.	73.0	63.0	51.0	37.0	32.0	27.0	23.0	19.0	15.8	13.2	11.0	8.8	5.6	3.2	2.0
B.	27.0	37.0	49.0	63.0	68.0	73.0	77.0	81.0	84.2	86.8	89.0	91.2	94.4	96.8	98.0

Place 3 Cc. of each of the mixed solutions in 100 by 10 mm. test-tubes, add 5 drops of 0.01% Phenolsulphonephthalein to each and seal off the tops. The series of colours so prepared represent different concentrations of Hydrogen-ions within limits likely to be found.

Collodion Sacs. The collodion is directed to be made by dissolving 1 ounce of Pyroxylin in Ether 250 Cc. and Alcohol 250 Cc. Allow to deposit and use the supernatant solution.

A good piece of glass tubing sealed off like a test-tube with internal diameter 9 by 120 mm. is used as a mould. Fill it with the collodion then invert it and pour out half the contents. Then place it upright and allow the collodion to fill the lower half again. Invert a second time and rotate on its vertical axis, the collodion being drained off. This must be done to render even. Now clamp the tube inverted and allow to stand 10 minutes, then soak bodily in water for 5 minutes. Loosen the upper rim with a knife and run a little water between the sac and the tube, gradually pull out the sac, and preserve under water.

To conduct the Determination :—

The assay must be done in a room free from fumes of acids or ammonia. Place 1 to 3 Cc. of clear serum or of blood to be tested in a sac which has been washed inside and out with 0.8% Sodium Chloride solution—the sac having been previously tested for leaks by filling it with the salt solution. Lower the sac into a test-tube 100 by 10 mm. inside diameter containing 2 Cc. of the salt solution until the fluid outside is as high as on the inside.

Dialyse for 5 to 10 minutes. Remove the sac and add 5 drops of the indicator, mixing thoroughly with the dialysate and compare colour with the set of standards against a white background.

The limits of error are very slight. The same results are obtained with 1 Cc. or 3 Cc. of blood, and it is immaterial whether there is 1 or 3 Cc. of salt solution. A mild case of acidosis gave an average of 7.55 on repeated examination using serum, and the oxalated whole blood from the same case gave an average of 7.25.

An account of the reaction and "buffers" of the blood.—A. V. Hill, B.M.J., i./22,340.

The Acid-Base equilibrium of Body-fluids. A revised nomenclature. The Hæmoglobin Committee of the Medical Research Council have issued a standardised nomenclature based on Hydrogen-Ion concentration—L. i./23,613.

H-ion concentration higher inside than outside the red blood corpuscle. Carbon Dioxide is not carried in the blood as a substance adsorbed to the hæmoglobin, but as a part of a physico-chemical system involving the Sodium Bicarbonate present.—Med. Res. Council, P.J. i./25,78.

HUMAN TISSUE ALKALINITY. Experimental and therapeutic alterations of, achieved by altering the ration of Carbonic Acid and Bicarbonate, either by modifying the CO_2 content, as in the case of overbreathing and direct inhalation, or by altering the Bicarbonate concentration by the ingestion of large doses of Sodium Bicarbonate, Sodium Acetate, Ammonium Chloride or Calcium Chloride.—J. B. S. Haldane, L. i./24,537.

A theory of œdema, on the grounds of increased acidity of the blood, has been put forward by Martin Fischer, but changes in H ion concentration produce not more than minute swellings, and other grounds suggest that œdema is really a phenomenon of osmosis.—Bayliss.

Application of Hydrogen-ion concentration in Biochemical problems. Important to take into account for growth of organisms, *e.g.* *B. Coli*, *Yeasts*, *B. Subtilis*, etc.—F. W. Gamble and N. Evers, P.J. i./22,175; L. i./22,1076.

For further data, see Gradwohl and Blaivas' "Blood and Urine Chemistry," 1920 (Kimpton); see also the original communications of Marriott, Levy and Rowntree, Arch. Int. Med. 1915, Vol. XVI., p. 389, and 1916, Vol. XVII., pp. 840—851. Prof. Haldane provides numerous references to the subject.—B.M.J., ii/19,295

Theoretical Notes on the Subject.

For a general consideration of methods of determining the Hydrogen Ion concentration of Solutions, see Chapter on Indicators.

HEMOCHROMATOSIS. An accumulation of free iron-containing pigment in the skin associated with interstitial fibrosis of liver and pancreas. In a certain number of cases glycosuria develops. The skin in exposed parts of the body shows brownish pigmentation. Liver more or less cirrhotic. Ascites may be present if cirrhosis is advanced.—J. S. Dunn, B.M.J. ii./21,783.

Saturated solution of Potassium Fluoride, in proportion of one drop to 5 Cc. fresh blood, prevents clotting and glycolytic action for at least a week.—B.M.J.E. i./24,40.

Calcium and other Inorganic Elements in Blood, Urine, etc.

Estimation of Calcium in Blood.

2 Cc. Ammonium Oxalate Solution (3.5%) are measured into a centrifuge tube, having a steep conical end, 1 Cc. serum is added and the contents stirred vigorously. Allow the tube to stand 2 to 3 hours and then centrifuge at 3,000 revs. per minute for 10 minutes. Pour off supernatant fluid and drain tube over filter paper. Add a further 2 Cc. Ammonium Oxalate solution and centrifuge again: remove Oxalate and centrifuge with a fresh 2 Cc. as before. Convert the precipitated Calcium Oxalate into Carbonate by passing through a Bunsen flame for one minute, any Ammonium Oxalate left being converted into Ammonium Carbonate and volatilised. After cooling, 1 Cc. of N/100 Phosphoric Acid is added and when solution is complete one drop (0.016 Cc.) of 0.04% Bromphenol Blue is added and titration carried out with N/50 Sodium Hydroxide, using a microburette or micrometer syringe. The end point corresponds with a colour intermediary between pH 4.0 and 4.2, and the difference between the titration figure so obtained, and that for the acid alone gives the amount of Calcium in the serum taken.

1 Cc. only of the serum need be taken, and results as accurate as 5% of the correct value have been obtained with 0.01 mgr. of Calcium per Cc.—J. W. Trevan and H. W. Bainbridge, *Biochem. Jl.*, '26,20,423-426.

1 Cc. N/100 Phosphoric Acid is equivalent to 0.64 mgr. Calcium Oxalate or 0.2 mgr. Calcium. Thus, 0.1 mgr. Calcium, which is a little more than the average content per Cc. of serum, would combine with 0.5 Cc. N/100 Phosphoric Acid.

The average serum-calcium value in normal children was found to be 10.4 mgr. per 100 Cc., and in cases with inflamed tonsils and adenoids, but good muscle tone, 9.8 mgr. as average. The average in cases with marked lack of muscle tone was 9.0 (range 6.6 to 10.6). Inorganic phosphates of the plasma in all cases were approximately normal though the Calcium values in the group with marked lack of muscle tone were more variable than the normal and groups with inflamed tonsils and adenoids but good muscle tone, no relationship between Calcium level in the blood and muscle hypotonus was established.—L. Wills, *B.M.J. i.*/25,302.

CHOLELITHIASIS. The Calcium content is often high. Normal 9 to 10 mgr. in 100 Cc. of blood. 30 patients were found to have over 11 mgr., 22 had normal, and 3 had a content below 9 mgr. Hypercalcaemia and hypercholesterolaemia almost coincide.—Sir B. Moynihan, *L. ii.*/26,794.

A nephelometric method of estimation of Calcium in blood and urine.—per *Pr.*, Feb. '26,176.

Blair Bell's Calcimeter for estimating Lime Salts in the blood, urine and other fluids.

In Blood.—The Calcium Oxalate crystals formed by mixing known volumes with Oxalic Acid are counted.

In Urine.—The lime is thrown out by a Reagent consisting of a Saturated Solution of Oxalic Acid in 5% Solution of Acetic Acid. The volume of the precipitate is compared in a specially graduated centrifuge tube with that produced with a Standard Solution of Calcium Phosphate $\text{Ca}_3(\text{PO}_4)_2$. *Details Edn. XVIII., Vol. II., p. 401.*

Menstruation is a periodic function only in so far as the Calcium metabolism is in harmony with this periodicity, and the function is dependent on Calcium metabolism in all its ramifications.—Sir James Barr, *B.M.J. i.*/09,517,592; *i.*/10,830; *i.*/12,878.

In most cases of exophthalmic goitre (thyroid secretion in excess) the Calcium index was low, hence administration of Calcium salts may be advantageous.

Determination by means of Ammonium Oxalate.—Y.B.P., 1922,34.

Potassium Content of the Blood.

Normal human serum contains somewhat less than 20 mgr. Potassium per 100 Cc., while whole blood contains about 8 to 10 times that amount.—Myers and Short, Y.B.P., 1922,36.

It was suggested that the Potassium content of the RED CORPUSCLES OF CANCEROUS PATIENTS (and of tumours) is higher than normal, but this is now doubted. We found as average 0.163% in 6 samples of entire blood.

Method of Estimation is provided, 18th Edn., Vol. II., p. 402.

Mean content was 20.3 mgr. per 100 Cc. An increase was found at the beginning of menstruation.—B.C.A., '28,A913.

The inorganic constituents of the blood.—O. L. V. de Wesselow, *L. i.*/24,1099.

Bound Phenols found in every normal blood in concentration of about 0.05 mgr. per 100 Cc. Large amounts and also free Phenols in pernicious anaemia, and a remarkable increase in the insufficiency stage of nephritis.—Jl. A.M.A., *i.*/25,1681.

Chemical tests of the blood—indications and interpretations with a collection of clinical aphorisms.—R. Rockwood, *Jl. A.M.A. ii.*/28,157.

A new non-protein substance, $\text{C}_8\text{H}_{11}\text{N}_2\text{O}_2$, believed to be simple Pyrimidine nucleoside isolated from pig's blood and is believed to be present in the blood of other animals. Its presence probably accounts for the higher Uric Acid values obtained by the direct method of Benedict than by the Folin and Wu process, the precipitation in the latter case effecting a separation.—Jl. Biol. Chem., '25,623, per Analyst, '26,95.

Blood Sugar Estimation.

Blood sugar can be determined by colorimetric or titration methods. The latter have the advantage of not requiring expensive apparatus.

Maclean's Method.

Of the blood, 0.2 Cc. is mixed with 23.8 Cc. of a solution containing 15% Sodium Sulphate and 0.1% (v/v) Acetic Acid. After raising to boiling and removing from a flame, 1 Cc. of Dialysed Iron solution is added, and, when cooled, the mixture is filtered through a Whatman paper, 20 Cc. of the filtrate being transferred to a 100 Cc. conical flask. Two Cc. of Standard Copper Solution (see below) are added and the mixture boiled for 6 minutes, cooled, and acidified with 2 Cc. of 25% Sulphuric Acid. In one minute the liberated Iodine is titrated with fresh N/400 Sodium Thiosulphate, using two drops of 1% soluble Starch Solution towards the end. The Standard Copper Solution is also similarly titrated against N/400 Thiosulphate by adding 2 Cc. of 25% Sulphuric Acid to a mixture of 2 Cc. of the Copper Solution and 5 Cc. of the Acid Sodium Sulphate Solution.

The difference between the two titration readings gives the Ccs. of Thio. due to the sugar and the percentage is read off from a table (v. Modern Methods in Diagnosis and Treatment of Glycosuria and Diabetes.—*Maclean*), or the amount can be calculated thus:—

$$\% \text{ Sugar} = (A \times 0.049) + 0.012$$

where $A = (\text{Cc. N/400 Thio. per 2 Cc. Copper solution} - \text{Cc. N/400 Thio. in experiment})$.

The Standard Copper Solution.—Should stand a few days before use. Potassium Bicarbonate 12 Gm. is dissolved by gentle heating (not above 37°) in about 60 Cc. Distilled Water, and Potassium Carbonate (anhydrous) 8 Gm. is added. Copper Sulphate (cryst.) 0.35 Gm., dissolved in a little water, is mixed with this, and when effervescence is over, after warming if necessary, to dissolve any insoluble Carbonate, Potassium Iodate 0.05 Gm. and Potassium Iodide 0.50 Gm. are added. The solution is then filtered through a starch-free paper and adjusted to 100 Cc. When titrated, as described, 2 Cc. should require about 11 Cc. of N/400 Thiosulphate.

For accurate work, the heating of this solution and the blood filtrate should be ensured by using the same burner and gas-pressure to bring the 22 Cc. of solution in the flask to vigorous boiling in 100 seconds.

The Cole Modification of the Maclean Method, using Metaphosphoric Acid as protein precipitant, does not seem to possess any distinct advantage, the original method being found entirely satisfactory.—G R. Lynch, L.i./23, 1180.

In adapting **S. W. Cole's Method** of estimating blood sugar to the slightly different conditions in the case of urine, no marked deviation from Cole's procedure is necessary, but strict adherence to technique is essential. 1. The interfering substances are removed by mixing equal volumes of urine and Patein and Dufau's reagent, rendering slightly alkaline with solid Sodium Bicarbonate and filtering. A slight excess of Sodium Sulphide solution is added to 10 Cc. of the filtrate, which is then made up to 100 Cc. and filtered. 1 Cc. of this filtrate will be equivalent to 0.05 Cc. of the urine. (Patein and Dufau's reagent: Dissolve by heat Red Mercuric Oxide 220 Gm. in Nitric Acid Conc. 160 Cc., and water 160 Cc. Cool, add 75 Cc. N/1 Sodium Hydroxide and make up to 1 litre.) 2. Determine approximately the sugar in the original urine by Benedict's, Nylander's, Fehling's, or Crismer's Sairanine reagents and take of the second filtrate quantities (ranging from 2 to 10 Cc.) inversely proportional to the amounts of sugar indicated, which would probably lie between 0.08% and 0.15%. 3. To this amount add 3 Cc. of Cole's alkaline Copper Iodate mixture and make up to 23 Cc. with water. Heat so that the solution boils in 2 minutes, and after boiling for exactly 8 minutes run in 5 Cc. B.P. dilute Sulphuric Acid, and remove flask from flame. Allow to cool

add two drops Potassium Iodide solution 10%, and estimate free Iodine with N/200 Sodium Thiosulphate, using a micro-burette and Starch as indicator. The difference between the number of Cc. of this used in the titration, and in a blank experiment with the alkaline Copper Iodate mixture gives the "Thiosulphate deficiency," from which can be calculated the % of reducing sugars present in the original urine, 1 Cc. of the Thiosulphate solution being equivalent to 0.035% reducing sugars, according to the table provided. (Cole's **Alkaline Copper Iodate Mixture**: Potassium Bicarbonate 20, Potassium Carbonate 30, Copper Sulphate 0.875, Potassium Iodate 0.075, Water to 250). The urine examined should be from a 24-hour sample, preserved if necessary with Toluol.—F. Wokes, P.J. ii./25,127.

The Folin and Wu Colorimetric Method (J. Biol. Chem., '19,38,81 and '20,41,367). This requires 0.2 Cc. of blood and consists of a protein precipitation with Tungstic Acid and estimation of the sugar with Phosphomolybdic Acid. Mackenzie Wallis and Gallagher applied the use of the torsion balance to this process, the blood being soaked up into a piece of filter paper weighed before and after impregnation.—L. ii./20,784.

Folin's Blood Tube, This is 20.5 cm. long and 2.3 cm. wide in the upper portion of 14 cm. Below this, its width is constricted to 0.9 cm. for 4 cm. length and terminates in a bulb about 2 cm. wide. Its capacity is 25 Cc.

Calvert's Modification is founded on the above methods. The blood is collected in a small Platinum capsule and weighed on a torsion balance. After removal of protein and treatment with alkaline Copper solution, Phosphomolybdic Acid is added. Unreduced Copper is decolorised and the Cuprous Oxide present dissolves, giving a deep blue solution, the colour being proportional to the sugar originally present. This solution is compared in a colorimeter with standard blue glass discs. It is claimed that the accuracy of the method is high.—Biochem. Jour., '23,17,177. See also B.M.J.E.i./25,10.

Kramer and Gittleman's Modification of Folin and Wu's method is simple—only 0.05 to 0.1 Cc. blood required. The blood is drawn into a fine pipette and mixed with 1.5 Cc. Distilled Water. Proteins are precipitated by adding 0.1 Cc. of 10% Sodium Tungstate solution followed by 0.1 Cc. of 1/3 N.H₂SO₄. This is well mixed, allowed to stand and centrifugalised. The supernatant liquor is pipetted off and transferred to a Folin-Wu tube. Two controls are prepared with standard Sugar solution. Alkaline Copper solution is added to all three, the tubes are heated, and 2 Cc. Phosphomolybdic Acid solution added to each. The contents are mixed and the colour compared. A calculation shows the sugar in mgr. per 100 Cc.—P.J. i./24,140.

The blue colour given by Phosphomolybdic Acid and Cuprous Oxide fades in time, and therefore colorimetric measurements must be made within an hour. Calvert's method criticised.—R. V. Stanford and A. H. H. Wheatley, Biochem. Jl., '24,18,22.

Hyperglycaemia and Glycosuria.—H. J. Hamburger, B.M.J. i./19,267.

Resorcin Method.—Colorimetric Assay by yellow colour given on boiling for 1 hour with 20% Hydrochloric Acid and excess of Resorcin.—I. B. Glassmann, Z. Physiol. Chim., 1925,150,16.

Time-saving points in the estimation of Glucose—use of **Dreyer's Pipette** (an ungraduated pipette which drops very consistently 22—24 drops of water to the cubic centimetre).—F. T. Grey, B.M.J. i./25,502.

Significance of Blood Sugar Content.—Generally speaking in health, the amount of blood sugar lies between 0.09 and 0.11%, except soon after a meal. With normal individuals, the ingestion of 50 Gm. of Glucose in 250 Cc. of water causes an increase, even to 0.18%, but the concentration falls back to normal in about 90 minutes. With diabetic patients there is usually a greater increase, but, of more importance in diagnosis, is a characteristic delay, often of many hours, before the sugar decreases to the usual value.—Maclean, *loc. cit.*)

Comparative determinations of blood sugar show that different values are obtained for blood in different parts of the circulation. It is suggested that blood is richer in sugar when circulating through active parts, and this is supported by the fact that blood from a paralysed limb is poorer in sugar than that from other parts of the body.—L. Pincussen and N. Klissiunis, Biochem. Zeit. '24,150,44 per J.C.S.A. i./24,1124.

In diabetic patients improving clinically it was found that the effect of the same dosage of Insulin was a more immediate, but smaller, drop in percentage of blood sugar, and the sugar started to increase in a shorter time after the injection. Subjects who showed a slight reaction to Epinephrin tended to give a relatively marked response to Insulin.—R. S. Lyman, E. Nicholls and W. S. McCann, *Jl. Ph. and Exp. Ther.*, Vol. XXI./23,365.

Diabetic sugar thought identical with normal blood sugar.—*Med. Res. Council*, P.J. i./25,78.

The blood sugar in cases of epilepsy.—I. De Burgh Daly, J. Pryde and J. Walker, *B.M.J.* 1./24,232.

Hypoglycæmia.—P. J. Cammdige, *L.* ii./24,1277.

Interrelationship of BLOOD FAT and blood sugar. Blood sugar appears to have a relation to the blood fat other than that of a mere oxidising agent. Fat, properly absorbed, appears to increase storage of carbohydrate; if not so absorbed, or if metabolised by Calcium, the storage is interfered with. Possibly, improper storage of fat may account for tendency of a high fat diet to produce glycosuria in some cases of diabetes.—T. H. Oliver and A. Haworth, *L.* ii./23,114.

Hellige Colorimeter.—For details of, see 'Blood and Urine Chemistry.'—Gradwohl & Blaivas, 1920.

A micro-chemical method of estimating.—R. S. Mackenzie Wallis & C. D. Gallagher, *L.* ii./20,784.

CEREBRO-SPINAL FLUID.

The composition is virtually that of Locke's Modification of Ringer's Solution. In examining a specimen centrifugalize or allow to stand for any sediment to deposit. Examine sediment for cells and Bacteria. Leucocytes indicate an acute process, *e.g.*, septic. Lymphocytes in excess—a chronic process such as tabes; tubercular meningitis, etc. Red corpuscles when in excess indicate hæmorrhage of meninges.

If the fluid be clear, test for Globulin by Salicyl Sulphonic Acid and other Tests.

Inoculate broth and other media for Bacteria.

Normal cerebro-spinal fluid is clear, colourless, and alkaline; the degree of alkalinity varies. By titration it is shown to be always diminished in infection. It becomes slightly turbid when boiled. The fluid may become coloured. Yellow fluid may indicate tuberculous or chronic meningitis, or tumour of the spinal cord; in subdural hæmorrhage or cerebral laceration it is red, but if the trauma be some days old the colour may be dark amber. Red colour may be due to accidental contamination; coagulation in the test tube is stated to be an infallible sign of this, but such a conclusion is not always justifiable. Turbidity is an indication of meningitis, but the fluid may be clear in subacute tuberculous meningitis. It is clear also in extradural hæmorrhage and in cerebral tumour.

A film made from normal cerebro-spinal fluid contains very few leucocytes and many fields may be examined before one corpuscle is found. Absence of leucocytes excludes meningeal inflammation, locomotor ataxy, and superficial gumma of the brain. It does not exclude cerebral abscess unaccompanied by meningitis; this shows the value of making a leucocyte count of the blood at the time the cerebro-spinal fluid is examined.

In pathological states the number of leucocytes is increased, and in inflammatory conditions a varying number of endothelial cells may be seen.

Sugar.—The fluid reduces Fehling's Solution. Normal sugar content varies from 40 to 77 mgr. per 100 Cc., or from 45—65% of the concentration in the blood. After ingestion of Dextrose, content in both fluids increased and the relation between the two changed. Low values for the sugar content were obtained in meningitis and in cerebro-spinal syphilis.—*J.C.S.* Ai./25,853.

In neurosyphilis, lethargic encephalitis, and other neurological conditions, the deviation of the sugar content is so slight as to be of no diagnostic significance, but in tuberculous meningitis it is below normal (*i.e.*, 60 to 90 mgr. per 100 Cc., with average of 83 mgr.) and in purulent meningitis it is frequently absent.—*B.M.J.E.* i./26,50.

Differential Diagnosis of Syphilitic from the Parasyphilitic affections by examination of cerebro-spinal fluid.

Normally the Fluid is practically free from corpuscular elements as stated *antea*—from 1 to 5 lymphocytes may be seen in the centrifugalised deposit in the ordinary microscopic field. In acute microbial infections of the cerebro-spinal meninges as by *staphylococcus*, *pneumococcus*, etc., leucocytosis occurs mostly of the polynuclear type.

In certain more chronic affections as in tubercle, trypanosomiasis and syphilis excess of leucocytes also occurs—mostly *mononuclear*, i.e., there is a lymphocytosis or pleocytosis. Tubercle bacillus and trypanosomes can usually be found, but the *Sp. Pallida* has not been found, in its ordinary form at least. The pleocytosis of cerebro-spinal syphilis, tabes and general paralysis is often a very early occurrence of great diagnostic value.

In florid syphilis and in cerebro-spinal syphilis as well as in tabes and general paralysis, the Wassermann reaction is practically always +.

The second reaction in *diagnosis of parasyphilitic affections* is the finding of an excess of globulin by the Nonne Apelt method:—Mix the cerebro-spinal fluid with Saturated Ammonium Sulphate Solution. Turbidity=excess of Globulin.

This always occurs in tabes, general paralysis and cerebro-spinal syphilis. In combination with a + Wassermann Reaction and pleocytosis it is pathognomonic of parasyphilis.

The third reaction is the pleocytosis; the fourth, is the Wassermann reaction, both already mentioned. The four reactions are relied upon for diagnosis. At least 95 to 100% of both tabes and general paralysis give a + reaction — using the latest method.—Hauptmann's Auswertung's Method.

Finally the great test is the therapeutical one. In cerebro-spinal syphilis Mercury or '606' in most cases will convert a + reaction to —. In parasyphilitic affections—tabes and general paralysis, this treatment is of no avail.—Sir David Ferrier, L. ii./13,1109.

Routine examination of cerebro-spinal fluid in syphilis.—C. H. Mills, B.M.J. ii./27,527. See also J. G. Greenfield, L. ii./28,716.

Colloidal Gold Reaction. Zsigmondy found that certain colloids exerted definite degrees of *protective action* on the precipitation of gold suspensions by Sodium Chloride. Lange applied the test to the C.S. fluid protein and found that normal fluid when diluted with a 0.4% Sodium Chloride solution does not affect the solution of colloidal gold, whilst in disease of the central nervous system characteristic changes are produced.

All cerebro-spinal fluids precipitate colloidal gold, provided that the gold solution is sufficiently sensitive, but, generally speaking, the precipitating substance is contained to a small degree in normal fluid, to a greater degree in tabetic cases, and to a still greater degree in paretic cases.—Med. Res. Com. Rep., 1919–20.

Technique:—Colloidal gold solution is red. Numbers are given to the colours formed on mixing the specimens with the gold, red=0, red-blue=1, violet=2, blue=3, bluish-white=4, and colourless=5. Ten dilutions are made varying from 1/10 to 1/5120. Results are given from left to right. In *general paralysis* a typical reading would be 5555554210 (the 'paretic curve'). In tabes the figures may be 222110000. In cerebro-spinal syphilis 1223320000 is fairly typical.—A. Douglas Bigland, L. ii./20,587.

Application of the test in disseminated sclerosis (during treatment with Novarsenobenzol). The usual procedure of dilutions 1:10, 1:20, 1:40 of fluid in 0.4% Sodium Chloride was adopted, and 2.5 Cc. Colloidal Gold was added to each tube. The colour changes were noted in 1 hour and in 24 hours. The criteria of the suitability of Colloidal Gold for testing cerebro-spinal fluid are (1) It must give a paretic curve with fluid from a case of general paralysis (2) Show no change with normal fluid (3) 5 Cc. should be completely precipitated in 1 hour by 1.7 Cc. of a 1% Sodium Chloride solution (4) It should be neutral to 1% Alizarin Red in 5% Alcohol.—D. K. Adams, L. i./21,420. (Med. Res. Council Report).

In disseminated sclerosis the test on the cerebro-spinal fluid almost invariably +. In 20 cases of functional nervous disease the cerebro-spinal fluid gave —. Apparently not specific, but of value to indicate first definite sign of involvement of the central nervous system in organic disease.—D. K. Adams, B.M.J. ii./21,842.

The reaction is of value for differentiating one pathological condition from

another, rather than as was first expected for making a quantitative determination of the protein.—*Physiology and Pathology of C.S. Fluid*, W. Boyd, 1920.
The test found to be in great measure specific.—*B.M.J.E.* i./20,32,68.

Preparation of the Gold Solution for the Reaction.

A number of slightly varied formulæ are available.

To 100 Cc. of triple distilled water add 1 Cc. of 1% solution of Gold and Sodium Chloride ($\text{AuCl}_3, \text{NaCl}$). Bring to the boil and add 10 drops of 1% Formalin. Remove partially from the flame and add 16 drops of 2% Potassium Carbonate Solution and then at intervals of 15 seconds one or two more drops: eighteen usually suffice. The colour should be a 'smart blush,' changing to old rose as it cools, with fluorescence. 5 Cc. will be rapidly decolorised by 1.7 Cc. of 1% Sodium Chloride and it will give luetic and parietic curves with appropriate positives and negative results with known negatives. Should not be used quite fresh but it may not on the other hand keep more than a week.—*T. Grey*, *B.M.J.* ii./22,1120; i./23,88.

Gettler and Jackson's method.—*Y.B.P.*, 1922,38.

A simplified method: One Cc. of 1% Gold Chloride and 1 Cc. of 2% Potassium Carbonate are added to 100 Cc. water. This is heated and as it begins to boil 1 Cc. of 0.5% Glucose is added and boiling continued. Fluid turns violet in a minute, and then purple, when it is removed for use.—*Y.B.P.*, 1922,38.

Benzoin Reaction for Syphilitic disease of the central nervous system.

One gramme of freshly powdered Sumatra Resin dissolved in 10 Cc. Absolute Alcohol; shake well and leave for 48 hours. Decant and add 0.3 Cc. of the clear fluid to 20 Cc. of *twice* distilled water at 35° C. For each fluid to be examined, a series of 6 or 12 test-tubes is to be put up. Into the first tube, 0.25 Cc. of Sodium Chloride solution (0.01%) is placed, and into remaining tubes 1 Cc. of saline. 0.75 Cc. of Cerebro-spinal fluid is measured into first tube, and 1 Cc. into second tube; 1 Cc. from the second tube is put into third tube and mixed; 1 Cc. from tube 3 put into tube 4, etc., until penultimate tube is reached, when, after mixing, 1 Cc. is discarded; last tube, containing only saline, acts as control. To each tube, including control, add 1 Cc. of the Gum Benzoin suspension and mix; leave for 12 hours. In reading, three degrees of precipitation are recognised, 0, 1, and 2. In the first no change occurs; the second shows some precipitation, but fluid remains opaque; the third shows complete precipitation with clear supernatant fluid. "Negative" or "Normal" readings, either no change whatever in all tubes, or precipitation in tubes 7 to 9 inclusive. A "Positive" reading is complete precipitation in all tubes, with sometimes a slight deviation in tubes 11, 10, or 9, and sometimes first tube remains opaque. Test nearly as sensitive as Wassermann to syphilis of the central nervous system. Positive result is not obtained with any disease other than syphilis of central nervous system.—*J. A. Braxton Hicks*, and *J. Pearce*, *B.M.J.* i./24,268.

Dilutions of the cerebro-spinal fluid (the final one being 1 in 16384 parts of saline) mixed with freshly prepared colloidal suspension of Gum Benzoin. Flocculation = + W.R.—*J. H. Dible*, *L.* i./22,1090.

Mastic Test (introduced by Emanuel) is on lines practically identical with the previous excepting that Mastic is used instead of Benzoin.

In positive cases complete precipitation of the Mastic occurs in a given number of tubes and results are read in the same way as the Colloidal Gold Test. When precipitation is complete the fluid becomes perfectly clear, and there is a heavy white deposit at the bottom of the tube.—"*Physiology and Pathology of the Cerebrospinal Fluid*," *William Boyd*, 1920.

Experiments with cerebro-spinal fluid.—*E. R. McDonagh*, *L.* ii./20,991.

The Benzoin and Mastic tests are of approximately equal value, but the Benzoin is simpler. In special cases, such as meningitis and multiple sclerosis, the Colloidal Gold test is preferable.—*Per J. A.M.A.* ii./25,1584.

The Benzoin Test preferred for ease of performance, etc.—*ibid.*, 1916.

A Colour Reaction in general paresis.

To 1 Cc. cerebro-spinal fluid add 0.3 Cc. Acetic Anhydride. Shake well and add drop by drop 0.8 Cc. Conc. Sulphuric Acid. Lilac tint indicates positive reaction; brown-yellow or red-yellow negative. Lilac tint appears immediately after addition of Sulphuric Acid, usually remaining about 5 minutes. Positive in 97% of cases of general paresis, and negative with almost every other type of mental disorder, except certain cases of neurosyphilis (other than general paralysis of the insane).—*J. S. Harris*, *B.M.J.* i./26,136.

Tryptophane Test.

In the diagnosis of tuberculous meningitis examine the cerebro-spinal fluid for Tryptophane as follows: Mix 2 to 3 Cc. of the fluid with 15 to 18 Cc. B.P. Hydrochloric Acid and 1 to 2 drops of 2% solution of Formalin. In 5 minutes add slowly down the side of the tube 25 to 30 drops of a 0.06% solution of Sodium Nitrite. A positive reaction is shown by a violet ring being formed at the point of contact.—per Pr., July '27,63.

FÆCES.

This is undertaken to determine the state of the various digestive functions, and to assist thereby the treatment of gastric and intestinal disease.

A trial diet is necessary. Various 'meals' have been suggested with the inclusion of Carmine, Carbon, etc., to mark the commencement. The author of this paper advises, however, ordinary meals during 48 hours as follows, to include (1) Milk undiluted or mixed with coffee, (2) Eggs, (3) Animal food such as fish, poultry, veal, beef, etc., (4) farinaceous foods—bread, potatoes, rice, (5) the various green vegetables and roots, (6) stewed fruit, (7) butter and various fats of meat.

The fæces are collected in a glass vessel—this permits macroscopic examination (constipation, etc.).

Bile. Secretion of. Stir a portion with concentrated aqueous Perchloride Solution. Normally after some hours all the portions containing *stercobilin* or *hydrobilirubin* take on a red colour, while those containing *bilirubin* take on green. An indistinct reaction shows that bile secretion is inhibited.

A normal stool when mixed with water or a solution of Mercuric Chloride remains turbid, but if **Soluble Albumin** be present the metal precipitates the protein and the precipitated albumin carries down with it the other particles in suspension in the fluid, so that the supernatant liquid on standing becomes clear.—R. Coope, L. ii./21,9.

Fermentation.—Set aside a portion in a fermenting flask.

Vibrios. A new method of isolating and cultivating from fæces, especially suited for detection of vibrio-carriers in field work. Place 250 Cc. sterilised tank water in enamel bowl with 1% common salt: add 1 Cc. 1% sterile Peptone solution immediately before inoculating medium with fæces. For collection and conveyance of stools large test-tubes (6 × 1 in.) are used containing 10—15 Cc. 1% salt solution. On arrival at laboratory, or after 2 to 6 hours at room temperature, 6 large loopfuls of surface liquids in tubes are inseminated. Test surface layer of bowls daily—in positive cases, vibrios as a rule appear in 2 or 3 days, and when abundant persist in bowls for 2 to 4 weeks.—J. W. Tomb and G. C. Maitra, I.M.G., Feb. '26,56.

Distinct gas evolution in twelve hours shows that **Starch Digestion** has not been satisfactory. The fæces in this case are distinctly acid—catarrhs affections of the small intestine. Gas evolution after 24 hours or later shows that the albuminous substances are being split up by the increased alkalinity of the fæces. In the former case there is **intestinal fermentation dyspepsia** and in the latter **intestinal decomposition dyspepsia**.

Fats.—All that is necessary is to determine the proportion of *split up* to *total fat*. The splitting up of fats takes place in the small intestine. One determines how much of the total fatty substance present in the fæces appears as *neutral fat*, how much as *soap*, and how much as *fatty acid*. Extract 2 to 3 Gm. in a Soxhlet with Absolute Alcohol, then with Chloroform for six hours. The residue on evaporation contains *all the fats*. Titrate with Alcoholic N_{10}^{10} KOH. Result: Fatty Acid + Soaps—the triglycerides being calculated as Stearic Acid, the No. of Cc. of Alkali $\times 0.0284$ gives the amount in Gm. of fatty acid and soaps (Acid Stearic M.W. = 284). The difference between total fat and fatty acid = neutral fat. About 75% of the fats ingested should be split up into soaps and fatty acids and the more the dissociation differs from the normal the greater the amount of neutral fats formed. The average amount of fat taken in health is 125 Gm. *p.d.* This would correspond normally to about 20 Gm. of total fat in the fæces. *The greater the amount of total fat the more defective the fat absorption.*

In pancreatic disease the fat content in the fæces is much increased.

Blood.—Benzidine may be used, *e.g.*, make an aqueous extractive filtered about 1=4. To about 2 to 3 Cc. add $\frac{1}{2}$ Cc. of 10 vol. H_2O_2 and then add 1 Cc. of 1% Benzidine Solution in 50% Acetic Acid and note blue colouration;

Rub up a piece the size of a walnut with equal volumes of Alcohol and Ether, filter and repeat until a colourless filtrate is obtained, then extract the residue with 4 Cc. of Glacial Acetic Acid and when this has drained off use a further 4 Cc. Shake out the combined filtrate with two or three times its volume of Ether and then with water *q.s.*, to make the separated liquids $\frac{1}{2}$ Ether layer and $\frac{1}{2}$ water. Run off the acid aqueous layer, wash the ethereal with water and then treat with 5 to 10 drops freshly made pale yellow Gualiacum Tincture and 20 drops of Hydrogen Peroxide. In presence of blood a blue to violet colour forms.

Blood and Soluble 'Albumin' in the Stools:—

Mayer's Phenolphthalin Reagent has been used for the first mentioned:—

Phenolphthalein 2 Gm., Potassium Hydroxide 20 Gm., water 100 Cc. Dissolve and add Zinc 10 Gm. and boil. Filter while hot (and decolorised). Keep in the dark with a little Zinc at the bottom.

In using, a small piece of fæces is taken from the middle of the stool after a milk diet and made into fine suspension by adding water if necessary. Fill a test-tube about one-third full with this. Add one-third of its volume glacial acetic acid, mix and boil and cool under tap. Add 5 Cc. Ether, mix well and set aside. Pipette off and add 1 Cc. of the reagent and a few drops of Hydrogen Peroxide. If blood present *immediate* deep red colour spreading down the tube.

Blood in water gives a positive reaction 1 in 500,000. A slightly modified form of the test employed. Copper even in traces interferes with the test.—J.C.S.A. ii./22,724.

Benzidine and Pyramidon Tests thought too delicate, giving a positive result when no pathological amount of blood is present: less than 1 in 30,000 to 1 in 20,000 of blood in the stools cannot be considered pathological. **Gregerson's Benzidine Test** is as follows. Prepare powder containing 0.2 Gm. Barium Peroxide and 0.025 Gm. Benzidine, dissolve powder at time of use in 5 Cc. 50% Acetic Acid solution. Smear a portion of fæces on to a glass slide and let a few drops of the solution run on the smear. If positive, a blue or green colour develops within a minute, and the reaction is graded according to depth of colour and the time taken to develop. A definite blue or green colour must develop within 30 seconds for a conclusive result. "Basted" foods, red bone marrow, underdone meat, and milk diet, may affect the test, but a positive result within 30 seconds is conclusive irrespective of diet.

In the **Pyramidon Test** an emulsion is made with a 'button' of fæces obtained from the centre of the stool, and 5 Cc. of water, to which a few drops of Glacial Acetic Acid are added, and the whole boiled. To an inch of this emulsion in a test-tube 16 drops Glacial Acetic Acid are added and 1 Cc. of a 5% Alcoholic solution of Pyramidon is gently poured down the side of the tube, forming a layer on top, and an equal volume of Hydrogen Peroxide is added in the same way. A positive reaction is shown by a deep blue colour developing within 15 seconds.—A. G. Ogilvie, B.M.J. i./27,755. See also *ibid*, 855.

Microscopic Examination.—The presence of *connective tissue* and *elastic fibres* indicates a defect in acidity of the gastric juice. Defective dissociation of connective tissue and coagulable proteins points to a primary gastric affection known as *achylia gastrica* (*Hayem's hypopepsia*). Appearance of elastic fibres, if not associated with connective tissue and coagulated protein, must be regarded as a sign of good gastric, but defective intestinal digestion. Considerable amount of undigested muscle fibre with well-marked contour may indicate bad intestinal digestion of meat.

For detection of *B. Tuberculosis* in, by Antiformin, *v. B. Tuberculosis*.

Cereal products, Vegetables, etc., can be recognised microscopically.

Starch.—Lugol's Solution detects. When unchanged and clumped together there is *deficient pancreatic enzyme*. On the other hand, *swollen granules* almost always indicate *catarrhal affection* of the small intestine where the digestion of the starches chiefly takes place.

Mucus.—Stain smear with 1% Sodium Alizarine Sulphate. Normal mucus appears as small flakes and scales faintly yellow. It is possible to determine the section of the intestine from which the mucus is derived by the tint of this colour—the further the distance from the anus the mucus has to travel the lighter the colour.

Detection of trypsin in the faeces to assist diagnosis of pancreatic disease. Rub up a small quantity with Glycerin, place on a serum plate and incubate at 55° to 60° C. for 24 hours, and note occurrence of depression in the medium. The reaction is not due to Pepsin. The amount of ferment was found to be distinctly greater in loose stools or diarrhoea, indicating that probably owing to the increased peristalsis the reabsorption or destruction of ferment is hindered and an increased quantity voided.

THE FÆCES IN ALIMENTARY DISORDERS.—For a consideration of the subject, control of diet, macro- and microscopic examination, etc., see R. Coope, L. ii./21,9; also Chalmers Watson *ibid.* 153; reply *ibid.* 362. The Bacteria present in the faeces are not for the most part dead, as commonly taught. Saccharose Milk Agar—a new medium apparently selective for intestinal bacteria.—D. Chalmers Watson, L. ii./22,127.

PLEURAL AND PERITONEAL FLUIDS.

Physical Characters.

Colour.—Note whether blood stained or not. (Caution: A small amount of blood may get into the fluid in the process of exploring.)

Observe whether transparent or otherwise.

Test for fat.

Consistence, Sp. Gr., odour, amount and nature of deposit are stated.

Chemical Investigation will give:—

(1) Reaction, (2) Presence of serum albumin and serum globulin, (3) Presence of Mucin or Nucleo-albumin by addition of Acetic Acid, (4) Sugar, (5) Urea for which the fluid must be concentrated to small bulk and all coagulated proteins be removed.

Microscopic Examination of Sediment.—For blood, epithelial cells, cancer cells, Foulis' cells (these are met with in fluids from malignant ovarian cysts or malignant peritonitis following such cysts), hooklets, crystals, actinomyces nodules, amœba dysenteriae.

General Characters.—It is difficult to tell a dropsical from an inflammatory fluid. It appears that the amount of proteins in an effusion depends much more upon site than upon cause. Pleural fluids contain the highest percentage of proteins, peritoneal fluids rather less and subcutaneous fluids very little. The fluid in cardiac dropsy is more highly albuminous than in dropsy of renal origin. Diagnostically all one can say is that a fluid with Sp. Gr. more than 1.018 containing more than 4% of Albumin is almost certainly inflammatory while one with Sp. Gr., less than 1.015 and an Albumin percentage less than 2½% is certainly dropsical. Fluid obtained by lumbar puncture in cases of cerebral tumour has a Sp. Gr., 1.006 and a Protein content of ½% in chronic cases up to 1 or 2% in acute stages.—For further details see R. Hutchison and H. Rainy "Clinical Methods."

STOMACH CONTENTS EXAMINATION.

An extended series of examinations proved that in a healthy subject food commences to pass the pylorus in from fifteen minutes to half an hour after ingestion, the time varying with the character of the food (e.g., carbohydrates leave the stomach before proteins), and the stomach is empty in five hours; The passage through the small intestine takes about three and a half to five hours, about one inch a minute, so that there is food in the cæcum before the whole meal has left the stomach.—H. W. Carson, Oct., Pr., 1912.

An **Outfit** is arranged containing the necessary **Reagents and Apparatus**. The **Reagents** include Blue Litmus Paper, Congo Red (an aniline colour turned blue by acids and red by alkali, the reverse of Litmus, indicates absence of Hydrochloric Acid in the stomach in cases of cancer, as weak Lactic Acid does not interfere), Benzopurpurin Paper, Alizarin Solution, Dimethyl-amido-azo-benzol Paper and Solution (an acid and alkali indicator which is not affected by Carbon Dioxide—a 1 in 500 Alcoholic Solution of the compound is used in ordinary chemical testing), Decinormal Soda Solution, Ether, Caustic

Potash Solution, Phenolphthalein* Solution (1 in Alcohol 90%, 300 with Distilled Water to 500, is reddened by alkali, but is not suitable for ammonia estimation), Cupric Sulphate Solution, Lugol's Solution, Methyl Green and Methyl Violet and other Test Solutions.

The **Stomach Tube** should have bevel-edged eyes, known as "velvet eye." Van Valsli's tube has the smaller eye of the two which should be on a level with and opposite the upper border of the other: this arrangement prevents possible blocking of the tube and injuring the lining of the stomach.

Aseptic Lubricant Glycerin Jelly, is used for assisting the passage of these tubes. A Glyco gelatin Pastil of Menthol, gr. $\frac{1}{12}$, with Cocaine Hydrochloride $\frac{1}{16}$ grain, is also useful to be sucked just before passing.

Dunham's Tassel consists of a little tassel of thread soaked in Dimethyl-amido-azobenzol Solution. It is attached to a thread, the patient swallows it, it is removed after an interval, and the resulting colour gives the condition of the stomach as regards free Hydrochloric Acid.

Turck's Capsule consists of a hard Gelatin Capsule, No. 00, enclosing a small rubber tube attached to a thread for withdrawing, and provided with strips of Congo Red, Blue Litmus and Dimethyl-amido-azobenzol papers; after swallowing and withdrawing, the resulting colours will be:—

1. If stomach contents neutral, no change in colour of any of the Papers.
2. If no free acid, but only combined acid and acid salts, the Litmus will be red and the others unaltered.
3. If there be free organic acid but no free Hydrochloric Acid, the Congo Red will be blackish blue, but the Dimethyl-amido-azobenzol Paper will be unchanged.
4. If free Hydrochloric Acid present, all the Papers will be changed—the Litmus red, the Congo Red blue, and the Dimethyl-amido-azobenzol Paper will be red.
5. If both Hydrochloric and Lactic Acid be present, the Congo Red Paper will have a blackish tinge.

The rubber tube will contain sufficient material for microscopic examination, *e.g.*, for the Oppler Boas Bacillus or Sarcinæ.

By means of a **Silver Stomach Bucket** a small quantity, *i.e.*, about 2 Cc. may be lifted up out of the stomach and examined. By **Turck's Aspirator Bottle**, which is exhausted by means of a bulb, the stomach contents flow into the bottle. This is one of the simplest methods of removing stomach contents.

The **Water Test** for myasthenia consists in introducing into the stomach 300 Cc. of water first thing in the morning, fasting, and 1½ hours afterwards another 100 Cc. containing 1% of glucose. In due course a small quantity of the stomach contents are removed and the sugar estimated from which is determined the amount of the original 300 Cc. remaining in the stomach.

Intiation of the stomach for diagnostic purposes is best carried out by the double bellows of a spray apparatus attached to a stomach tube. A method of inflation is by giving first Tartaric Acid, 30 to 90 grains in water, followed immediately by 40 to 120 grains of Sodium Bicarbonate, and another is by Auto-inflation by means of Spivate's tube.

Portions of stomach contents are removed to examine for acidity, to ascertain the presence of food, mucus or gastric secretion, when it should normally be empty; to examine test meals and to search for pus, blood and bacteria.

***Thymolphthalein**.—Dissolves in caustic alkalis forming a blue colour, may, therefore, be used as an indicator—is not affected by excess. To prepare, heat Thymol 3, Zinc Chloride 2.5 and Phthalic Anhydride 3, for 6 hours at 115 to 120° C. Break up when cold and remove Thymol with Steam. Dissolve in Caustic Soda and pour solution into dilute Hydrochloric Acid, wash precipitate with water and crystallise from Alcohol.—P.J. ii./13,881.

The use of **Thymolsulphonaphthalein** has many advantages as an **Indicator in acidimetry** owing to the fact that it shows two distinct changes of colour at different hydrion concentrations. It may be used for the differential titration of mixtures of weak and strong acids, *e.g.*, Benzoic and Hydrochloric or Acetic and Sulphuric, although in the last the error may be as much as + or — 0.5%. It can be used to titrate Aniline with Hydrochloric Acid,—Abst. Ann. Rep. Chem. Soc., 1919 (Vol. XV.), p. 132.

For further details see Chapter on Indicators and p. 416;

Ewald's Test Breakfast consists of two or three ounces of dry bread and 10 ounces of hot water, or weak tea without milk or sugar. The Lactic Acid in bread vitiates the results where the presence of this acid is of importance, as in the early stages of cancer.

Boas's Test Breakfast (given after lavage) consists of one full tablespoonful of oatmeal to a quart of water, reduced to a pint by boiling. There are a variety of other test (meat and bread) meals.

The following are abstracts from the works of Willcox, Herschell, Martin and others:—

Chemical Examination of the gastric contents after a test meal, containing little protein and nitrogenous bases.—Willcox.

The Hydrochloric Acid in this case will be present as far as possible in the free condition (which is the point of importance in diagnosis of gastric ulcer).

I. Total Acidity (Normally = 0.15% HCl). Determine whether there is active Hydrochloric Acid or a mixture of this and organic acid. Usually in chronic gastritis acidity is low. In *gastric ulcer it is high*. In *carcinoma it is usually low*. (A normal acidity does not exclude gastric carcinoma.)

It is increased in simple hyperchlorhydria, peptic ulcer, cholelithiasis, appendicitis, and colitis.—L. i./13,462.

Increase in the mineral Chlorides may be an earlier sign of carcinoma than the diminution of the active acid. The condition may be accounted for by the secretion of an alkaline fluid in the stomach—probably by a malignant growth that has begun to ulcerate.—Q. Jl. Med., Apl., 1911, 334.

Without doubt both total acidity and free Hydrochloric Acid are raised in a considerable proportion of ulcer cases. Duodenal cases show on an average a larger and more constant increase of acidity than the ulcers on the gastric side. Discussion on gastric ulcer.—B.M.J. ii./12,940, *et seq.*

Litmus Paper is affected by Hydrochloric, Lactic and Butyric Acids.

Congo Red Paper—As already stated—the colour caused by organic acids will disappear on warming over spirit lamp whilst that due to Hydrochloric acid remains.

II. Hydrochloric Acid. This, according to Willcox, is either (a) **free**, (b) **combined** with protein and organic bases (*i.e.*, **physiologically active**), or (c) **Inorganically combined** (*i.e.*, **physiologically inactive**). Normally free HCl is 0.1%.

(a) **Phloroglucin test for free Hydrochloric Acid** (Gunzburg):—

Phloroglucin 2 Gm., Vanillin* 1 Gm., Alcohol 90% 30 Gm. A rose red colour formed on warming a few drops with an equal amount of the specimen in a porcelain dish indicates presence of the Acid. May also be best kept in powder form—2 parts of Phloroglucin and 1 part of Vanillin. As much as will lie on the point of a penknife, added to a few drops of alcohol, forms a perfectly reliable solution. This is the most trustworthy.

This test is positive with free mineral acids and may be relied on to show the absence of Free Hydrochloric Acid.—L. ii./12,1104.

Resorcin will do instead of Phloroglucin—a few crystals of this and of Vanillin dissolved in a drop of the test meal and evaporated to dryness give a clear result.—Slightly more purple than with Phloroglucin. The result is positive with very dilute Hydrochloric Acid in protein solution, and negative with combined Hydrochloric Acid and with Lactic Acid.—P. N. Panton, L. ii./18,125.

Response to †**Dimethylamidoazobenzol** may be given by organic acids

* **Vanilla Extract.** A menstruum, containing 47—50% of Alcohol, will produce the best Vanilla Extract, as regards clearness, colour and flavour.—P.R. '24,257. Vanillin, Piperonal and Coumarin Estimation.—L. Radcliffe and E. Sharples, P.R. '24,396,437. A patent specification for the preparation of Vanillin is based on using the condensation product of Guaiacol and Chloral Hydrate. The Guaiacyltri-chloromethyl Carbinol obtained is hydrolised, and the acids obtained are oxidised to Vanillin.—P.R. '24,288. See also P. May, P.R. '24,351.

†**Dimethyl-amino-azo-benzine** is red at P^H 2.9 and yellow at P^H 4.0. A 0.2% solution in 90% Alcohol is employed.

if these are present in large amount. The latter may be used first, followed by Gunzburg's test as confirmatory. If the test meal has been such as to give the Hydrochloric Acid the opportunity of being present in the free condition, then in normal gastric contents it will usually be present.

In *gastric ulcer* and *hyperchlorhydria* Free Hydrochloric Acid is always present; in *carcinoma* scarcely ever present.

(Lignified Tissue moistened with a little Hydrochloric Acid, then a little Phloroglucin applied, gives the well-known crimson colour. The author has found that RESORCIN moistened with Hydrochloric Acid gives a purple colour with pine wood (also with oak and teak, but not so rapidly), and with newspaper made from wood pulp, but Resorcin gives no colour with linen papers.)

Boas' Test for Free Hydrochloric Acid.—Resorcin 5, Cane Sugar 3, Alcohol 100. This test is used exactly as Gunzburg's test, the same red color being produced, but Boas' requires heating more carefully, as it chars more readily and the color is not permanent.

(b) **Physiologically Active Hydrochloric Acid, i.e., Free and combined** with protein and organic bases (normally about 0.15%)

Willcox's Modified Volhard Method.

Two equal quantities (20 Cc.) of gastric contents are taken and in one the total chlorides is estimated by adding excess N/10 Silver Nitrate and titrating back with Ammonium Sulphocyanide. From the other quantity free HCl and the acid combined with organic Nitrogen compounds is removed by evaporation and gentle ignition, the remaining inorganic chlorides being then determined as before. Difference gives *Active HCl*. In gastric ulcer and hyperchlorhydria the Active HCl is equal to or nearly equal to the total acidity, and is usually over 0.15%. In gastric carcinoma the Active HCl, as found by Willcox, is nearly always much reduced.—always under 0.1%. In chronic gastritis the Active HCl is often below normal.

Differential Estimation of Physiologically Combined and the Free Acid.

The fluid is titrated with Alkali in presence of Dimethyl-amidoazobenzol as indicator, the result being the physiologically combined + Free Hydrochloric Acid; then another portion is titrated with Alizarin Red (1% Aqueous Solution) as indicator, which gives Free Hydrochloric Acid only. The amount of alkali required in first titration minus the amount required for the second titration is the amount required by the *Physiologically Combined Hydrochloric Acid, i.e., Hydrochloric Acid combined with proteins and other weak bases, e.g.,*

1st titration showed 0.2% calculated as Hydrochloric Acid.

2nd titration showed 0.15% Free Hydrochloric Acid.

$0.2 - 0.15 = 0.05\%$ Physiologically Combined Hydrochloric Acid.

Total chloride concentration and acidity of the gastric contents.—B.C.A. '28, A1153.

Thymol Blue (Thymolsulphonephthalein) as indicator for gastric contents examination. The free Hydrochloric Acid is determined by the first change at $\text{pH } 2$ and the total acid by the change at $\text{pH } 8.8$.—S. W. Cole and W. J. Adie, L. i./21,423. See also p. 414.

It is suggested to retain Dimethyl-amino-azo-benzene, since most of the data has been obtained with this indicator, and in some cases the acidity, although considerable, might not be high enough to effect the first colour change of Thymol Blue.—J. T. H. Ryffel, L. i./21,536, see also *ibid* 778.

The active Hydrochloric Acid, according to Willcox, is best titrated by the modified Silver Nitrate titration method (described above) of Lancet, June, 1905.—L. i./24,594.

III. Organic Acid, Lactic Acid. According to Willcox great importance should not be attached to presence or absence of this acid. Organic Acids in considerable amount are present in carcinoma of the stomach and where much fermentation is going on.

Uffelmann's Test for Lactic Acid—(not entirely satisfactory). Ferric Chloride Solution 1 drop, Phenol 0.4 Gm., water to 50 Cc. (Delicacy limit 1 : 10,000—the violet colour changes to yellow.)

An approximate estimation may be conducted as follows:—

Distil off 30 Cc. from 40 Cc. of the filtered stomach contents the total acidity of which is known. The volatile acids go over; the residue contains the Lactic and Hydrochloric Acids. The acidity of the distillate (found by titration with

N/10 Soda, using Phenolphthalein as indicator) deducted from the total acidity "A" (found by titrating 10 Cc. of the filtered stomach contents in the same manner, the result being expressed in terms of Hydrochloric Acid) gives the amount of Lactic and Hydrochloric Acids together. If the amount of HCl "H" (found in the same way as "A," but using Dimethyl-amido-azobenzol as indicator) be deducted from this, the remainder is **Lactic Acid**.

IV. Mucin. Important. In gastric ulcer and hyperchlorhydria usually absent. In gastric carcinoma a definite precipitate occurs on adding 2% Acetic Acid. In simple gastritis often present in small amount.—Willcox. It is soluble in Sodium Hydrate Solution. Dried film is deeply stained reddish violet by Thionin Staining Solution.

Mucus normally is stained faintly, but that met with in chronic gastritis deeply with Methyl Green.

Blood is recognised microscopically.

Ferment Activity. Determination of Pepsin and pepsinogen present is of great importance. The method of Willcox is as follows:—

Action on milk by determination of the activity of the gastric juice by **Rennin** contained (usually proportionate to Pepsin) by using a series of tubes containing 5 Cc. of milk, to which are added gradually increased quantities of the gastric juice, and the mixtures maintained at 40° C. for 30 minutes. About 0.2 Cc. of normal gastric juice (of the adult) is required in this test.

In *gastric carcinoma* much more.

In *gastric ulcer* and hyperchlorhydria usually less (0.05 or less)

In certain cases it may be necessary to estimate **Renninogen**,—consult the paper.

Rennin is tested for by adding a few drops of the filtered and neutralised stomach contents to two or three Cc. of milk and maintaining the mixture at 98° F. for a quarter of an hour, resulting coagulation indicates presence.

For testing for **Rennin Zymogen**, a small quantity of Calcium Chloride is added prior to incubation. A pocket incubator may be used for these experiments.

Digestive activity of the stomach contents (*i.e.*, amount of Pepsin secreted) increases or diminishes with the amount of Hydrochloric Acid secreted by the mucous membrane. A number of cases of gastric carcinoma compared with cases of ulcer and functional disease showed that on the whole the greater proportion of cases evidenced a great diminution of acid secreted, as well as diminution of digestive power.—S. Martin. L. i./09,398.

The pain of GASTRIC ULCER has been attributed to an excess of Hydrochloric Acid acting on the affected membrane. 0.5% Hydrochloric Acid applied to an abrasion of the skin produces smarting and might be expected to cause pain in a gastric ulcer, but was quite tolerated when 4 ounces were introduced into the empty stomach by a tube where gastric ulcer was subsequently diagnosed by operation. Similarly HEARTBURN has often been ascribed to the regurgitation of the Hydrochloric Acid into the œsophagus, but some observations negatived this also: nevertheless the Acid is in some way evidently connected with the production of the pain, as Alkali relieves it.—L. i./11,1215.

Nitrogen Factor.

The Phenolphthalein and Dimethylamidoazo-benzene readings of acidity are employed to give what is termed the Nitrogen Factor. In an active stomach "*Phenol*" minus "*Dimethyl*" reading is a constant under Normal Test Nitrogen meals, etc. A certain multiple of this constant—the Nitrogen Factor is normally about 2.4. A rise above this indicates stasis or impairment of the digestive process. Table of 19 cases presenting appendicular disturbance.—C. Singer, L. ii./12,1711.

Test for the products of **Starch Digestion**. The presence of Erythro-dextrin in any quantity (giving a brown colour with Lugol's Solution) one hour after a test breakfast will point to hypochlorhydria.

Gunzburg's Capsule, for testing digestive power, consists of $\frac{5}{8}$ inch of thin rubber tubing, $\frac{1}{8}$ inch in diameter, containing $1\frac{1}{2}$ gr. Potassium Iodide plugged with pledgets of Fibrin at each end.

Fermentation is examined by means of an ordinary Doremus Ureometer.

Estimation of the **digestive power** of the gastric juice is effected with hard boiled egg by examining for peptone after two hours or so at 40° C.

Peptic Index ascertained by means of **Edestin**, a substance made from Linseed, purified by recrystallisation from warm salt solution. It is soluble 1 in 60 of 0.2% Hydrochloric Acid, 1 in 25 of 0.5% Sodium Hydrate, about 1 in 460 of 4% Sodium Chloride.

Employed as diagnostic in a variety of diseases.—B.M.J. ii./13,885.

Keratin Coated Hard Gelatin Capsules (largest size) filled with **Bismuth Carbonate**, and **Chain Cachets** (2 inches of fine silver chain in a cachet attached to a piece of silk), are used for **X Ray examination** of the stomach. Barium Sulphate and Bismuth are also used, cf *Vol. I.*, pp. 222, 228, 232.

Microscopic Examination reveals starch, sarcinæ and the **Oppler Boas Bacillus**, present in malignant disease—stained with Methylene Blue. (It is Gram + staining.)

Gastric function in health and disease.—J. A. Ryle, L.i./25,583,641,697,754.

The technique and clinical interpretation of the fractional method of gastric analysis.—L. M. Morris, Jl. R.N.M.S., Apl. '26,89.

Tropæoline OO and **Methyl Orange** (Helianthin), *e.g.*, as Solution—Methyl Orange 0.4, Alcohol (90%) 50, Water to 200, are yellow colours used for testing for the presence of free acids. The former is changed to crimson by acids, the latter to pink, but no change is produced by Carbon Dioxide, Acid Carbonates or Metallic Salts. They are not suitable for Organic Acids. Acid Phosphates, *e.g.*, NaH_2PO_4 are not acid to Methyl Orange.

Rosolic Acid. *Syn.* AURIN, CORALLIN.

1% in 60% Alcohol. Turns rose red with alkalis and yellow with acid. Remove CO_2 . It is not suitable in presence of NH_3 .

See also Table of Indicators.

WATER ANALYSIS NOTES (CHEMICAL).

Work in an atmosphere ammonia-free. The sample of Water should be received in a 'chemically clean' Winchester quart-stoppered bottle, and dated.

Note **Physical Characters**, smell, sediment, and colour in a 3 feet tube.

Total Solids are ascertained by evaporating 100 Cc. in a platinum basin on the water-bath, the result being expressed in parts per 100,000 or grains per gallon (parts per 70,000). The quantity being determined, it is essential that the amount of volatile and non-volatile matter should be determined, or, in other words, the amount of organic and inorganic solids, or those that will disappear on ignition and those that will not. (Some of the inorganic solids, *e.g.* Magnesium Carbonate, Calcium Nitrate, will also be decomposed on ignition.) Also notice the appearance on ignition, *i.e.*, charring (indicating organic matter), fuming, scintillation, &c.

Oxygen Absorbed.—Warm $\frac{1}{2}$ litre of the sample about 20 minutes in a flask with 1 Gm. Ferrous Ammonium Sulphate $\text{FeSO}_4(\text{NH}_4)_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$ acidified with dilute Sulphuric Acid, then back-titrate with N/10 Potassium Permanganate.

Free and Albuminoid Ammonia.—Prepare some water, NH_3 free, by acidulating some good tap water with Sulphuric Acid, about 2 drops of a 1 in 3 solution to a litre of water and distilling. By so doing (the retort and condenser being chemically clean) even the first drop of distillate is Ammonia-free. Distillation may proceed, but must not be pushed too far. The distillate should be Nesslerised to verify its purity. Take 500 Cc. of sample in a boiling flask with rubber cork to connect with condenser. Distil 200 Cc., Nesslerising each 50 Cc. of distillate with standard NH_4Cl of which 1 Cc. = 0.01 mg. NH_3 . Add together the equivalent quantities of NH_3 and double the result to arrive at number of mgrs. of **Free Ammonia** per litre = parts per million. Then add 50 Cc. of a solution of 0.4 Gm. Potassium Permanganate and 10 Gm. Potassium Hydrate which has been freshly boiled 20 minutes. Distil again and Nesslerise the **Albuminoid Ammonia** in 50 Cc. of the distillate at a time until it is NH_3 free. Add the equivalents together and double as above for parts per million.

Wanklyn divides waters in the following:—

Class I. Of extraordinary purity, yielding from 0.00 to 0.05 part per million of Albuminoid Ammonia, which cannot be objected to organically.

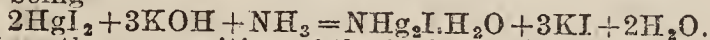
Class II. The general drinking waters of this country, containing 0.05 to 0.10 part Albuminoid Ammonia per million—this amount may be considered safe organically.

Class III. Dirty waters, yielding more than 0.10 part of Albuminoid Ammonia per million.

(P) Nessler's Reagent for Ammonia. *Syn.* SOLUTION OF POTASSIO MERCURIC IODIDE.

Dissolve Potassium Iodide 7 and Mercuric Chloride $2\frac{1}{2}$, in Distilled Water 160. To this add more of the Mercuric Chloride in solution until the precipitate no longer disappears on well stirring, and a slight permanent precipitate remains. Then add Sodium Hydroxide 24, dissolve, add a little more solution of Mercuric Chloride and Distilled Water *q.s.* to 200.

On the addition of this test to ammonia or an ammonium salt in solution, it lets fall a brown precipitate which may be Di-mercuric Ammonium Iodide the equation being



Schmidt gives the composition of the body precipitated as $\text{HgINH}_2 + \text{HgO}$ —a basic Mercury-Ammonium Iodide.

Nessler's Reagent (Richmond's Formula).

A very sensitive reagent may be made by mixing a solution of 17.5 Gm. of Potassium Iodide in 100 Cc. water with 15 Gm. Mercuric Chloride in 300 Cc. water, thoroughly washing precipitate by decantation, and dissolving in 17.5 Gm. Potassium Iodide in 100 Cc. water. A few drops of Mercuric Chloride solution are then added until a precipitate insoluble on shaking is formed; the mixture is diluted to about 500 Cc., cooled in ice and mixed with a solution of 105 Gm. Sodium Hydroxide in 250 Cc. The mixture is made up to 1 litre and allowed to settle.—H. D. Richmond, *per P.J. ii./25,394. We have tried this formula and found it satisfactory—it is far more delicate than the B.P. '14 formula. For a further Modification see p. 385.*

Estimation of Ammonia in Water in presence of Hydrogen Sulphide.

The presence of Hydrogen Sulphide in a water interferes with the Nessler test. If the amount of Ammonia be large the Sulphide may be precipitated with a Zinc or Lead Salt and the Ammonia can then be estimated directly by the Nessler Reagent. If the amount is small it is best to add to 500 Cc. of the water, a measured quantity of N Sulphuric Acid and distil 100 Cc.,—this completely removes H_2S . A volume of $\text{N}/1$ NaOH equal to that of the H_2SO_4 used is now added. The water is again distilled until 200 Cc. have collected and the Nessler test is applied to the distillate.

Chlorine. Titrate 100 Cc. in a white basin with standard AgNO_3 of which 1 Cc. = 1 mgr. of Chlorine, using potassium chromate as indicator. The reagents must be Cl-free and the water must not have an acid reaction. The average content is about 2 parts per 100,000, though frequently one finds a content of 5 to 15 parts per 100,000. It should be remembered that urine and sewage are, comparatively speaking, highly charged with chlorine—this enables the analyst to determine whether a high albuminoid Ammonia content is attributable to sewage or vegetable influence. *Per contra* almost entire absence of chlorides, coupled with excess of Albuminoid Ammonia, and little free Ammonia suggests vegetable contamination of a dangerous character. One frequently obtains waters for examination with an exceedingly high Cl-content in conjunction with an almost total absence of organic impurity. Such waters, though 'saline,' are suitable for drinking purposes.

Nitrites. To 100 Cc. of the sample add a weak, slightly acidulated, colourless solution of Meta-phenylenediamine. Nitrites give an amber to mahogany colour according to the amount. Conduct a control experiment.

Neutral Red Test. To 10 Cc. of water add 1 Cc. of a 0.0025% aqueous solution of Neutral Red followed by 3 Cc. of dilute sulphuric acid. A deep blue colour indicates nitrites, .005 mgm. per litre shows. The test is not affected by presence of iron, manganese or other metallic salts which occur in natural waters.—J.C.S.A. ii./23,505. We found this satisfactory.

Resorcin Test. Prepare a reagent by dissolving Resorcin 3 Gm. in pure Sulphuric Acid 50 Cc., giving a pale greenish-yellow solution. Fill a test-tube with the water to be tested to about two-thirds full, and run 3 or 4 Cc.

of reagent down the side, without mixing. In presence of nitrites a pink ring is formed. The test can be made quantitative by matching with a known Sodium Nitrite solution and reading result after 20 minutes.—Y.B.P. '23, 175.

Nitrates. The test employed is to mix 1 part of saturated solution of a Brucine Salt with 3 parts of the specimen, and to "layer" beneath this carefully 1 part of pure Sulphuric Solution—a pink colouration indicates their presence.

Diphenylamine (C_6H_5)₂NH = 169.096 in 1% solution in sulphuric acid is a very delicate test for nitric acid, giving a blue ring on properly layering.

In the basic condition it is practically insoluble in water and soluble about 1 in 8 of alcohol, 90%.

Diphenylamine Reagent 'A.R.' Dissolve Diphenylamine 0.085 Gm. in 190 Cc. of dilute Sulphuric Acid (1 : 3) and when cold make up to 500 Cc. with strong sulphuric acid.

Nitrates, determination.

(1) Improved Phenolsulphonic Acid Method.

The Phenolsulphonic Acid Reagent is prepared by heating 4 Gm. Phenol with 4 Cc. of water and 100 Cc. of concentrated Sulphuric Acid for 6 hours at 80—85° C., adding Sulphuric Acid to 500 Cc., and then diluting to a litre with a mixture of 200 Cc. of water and 300 Cc. of Sulphuric Acid.

To 25 Cc. of the sample is added 2 Cc. of the reagent and water is removed by evaporation. The residue is twice dissolved in about 10 Cc. of water, and evaporated as dry as possible. It is then taken up in 95 Cc. of water and 3 Cc. of 0.880 Ammonia is added. The colour is compared with that obtained by similarly treating a standard solution of Potassium Nitrate containing 0.1 mgm. of N as nitrate.—R. C. Frederick, Analyst, 1919, p. 281.

(2) Mayrhofer's Method.

5 Cc. of concentrated Sulphuric Acid is run into 5 Cc. of the water and the mixture is titrated with standard Indigo solution, the titre of which is determined by means of a solution containing 0.0962 Gm. Potassium Nitrate (\equiv 0.06 Gm. Nitric Acid) and 1 Gm. of Sodium Chloride per litre.—Analyst, 1922, p. 311.

Nitrates and nitrites can be estimated as Ammonia by Nesslerising after reduction with the Zinc-Copper couple.

Sulphates. The estimation of these is relatively seldom required. A volume of the water may be concentrated and precipitated with Barium Chloride in HCl. solution in the usual way. A new method employing Benzidine is given.—P.J. ii./15, 139.

Total Hardness.—To 100 Cc. of specimen add the least amount of soap solution (standardised so that 1 Cc. = 1 mgm. Calcium Carbonate or its equivalent) that will give a lather which will have an unbroken surface at the end of 5 minutes. 1 Cc. of the soap solution must be deducted from the amount required, as 100 Cc. of Distilled Water would require 1 Cc. to furnish a lather. The number of Cc. of soap solution required gives the number of mgm. of Calcium Carbonate in the 100 Cc. of the specimen or the parts per 100,000.

Standard Soap Solution for the above determination:—Dissolve 10 Gm. of Hard Soap in 1 litre Alcohol 35%. 1 Cc. of this solution will contain soap approximately equivalent to 1 mgr. $CaCO_3$. To standardise to this equivalent dissolve 1 Gm. Powdered Marble or Calcium Carbonate in slight excess of Hydrochloric Acid, evaporate to dryness and redissolve in distilled Water, *q.s.*, to 1 litre. Take, say, 12 Cc. of this solution, add Water to 100 Cc., and then Soap Solution, *q.s.*, to form lather as above. Adjust the Soap Solution until 13 Cc. are required. (100 Cc. of distilled water alone would consume approximately 1 Cc. of the Soap Solution in forming a lather.) We find London tap water varies between 15° and 17°.

Poisonous Metals.—Concentrate the water 5 times after acidulating with two drops of Hydrochloric Acid. Add Ammonium Sulphydrate solution. A darkening indicates Pb, Cu, or Fe, but not Zn. This darkened water should be divided into two parts. To one add Hydrochloric Acid—if darkness goes Fe is present. To the other portion add Potassium Cyanide Solution. If darkness goes now the metal is Cu; if it does not, it must be Pb. This latter proceeding is, of course, only necessary when the darkness does not go with

Hydrochloric Acid. Confirmatory tests should always be employed. The confirmatory test for Fe and Cu is, to some original concentrated water in a test tube add Hydrochloric Acid and Potassium Ferrocyanide; a blue results with Fe, and a bronze with Cu. For Pb the Potassium Chromate test is employed. Zn gives a white precipitate with Ammonium Sulphhydrate, and a white precipitate with Hydrochloric Acid and Potassium Ferrocyanide. See also Details for *Army purposes, infra*.

A pure soft water may act upon zinc, *e.g.*, on galvanised kettles, in a solvent way, so as to become dangerous to health.

Electrolysis of lead water pipes, owing to leak of 1.8 volts in earthed returns of electric cable, has resulted in contamination of the water.

ZINC in small quantities is found in soft waters passing through galvanised iron pipes. From the health aspect and danger of poisoning from, it can be ignored.—J. C. Thresh, L. ii./15,1098. See also B.M.J. i./15,80 (Park Prewett).

Lead in Peaty and other waters.

EXCESSIVELY PURE WATER may be solvent of lead in service water. It is recommended to harden it by adding lime.

PEATY WATERS owing to *acidity* often dissolve lead from main pipes in the form of lead hydrogen carbonate. On standing or on boiling, it is thrown out with the calcium carbonate.

LEAD-ABSORPTION from drinking water. 120 cases.—L. ii./14,213.

Owing to the brown colours of Peaty waters, it is best to oxidise with Potassium Permanganate first, adding sufficient quantity to render distinctly pink; then render alkaline with Ammonia and keep for about 48 hours. The precipitate contains all the lead. Collect it on a filter, solve in a few drops of strong Hydrochloric Acid and test after dilution with Alkali Sulphide in the usual way.—T. Tickle, Analyst, 1921,46,240; Y.B.P. '22,130.

Determination of minute amounts in water by concentration, dissolving the Hydrogen Sulphide precipitate in Nitric Acid and precipitating as Lead Sulphate.—Y.B.P., '22,126.

Plumbo-solvent waters.—B.M.J. ii./26,764.

Sodium Silicate added to water supplies, with the object of eliminating plumbo-solvent action. Unsited to soft acid waters.—T. D. Harries, B.M.J. ii./27,40; *see also ibid* 80.

CHALKY WATER.—Public (and often other) opinion is to the effect that chalky drinking waters may be responsible for a variety of complaints *e.g.* gout, rheumatism, calculus, constipation, biliousness, dyspepsia, eczema, goitre and arteriosclerosis. P. G. Lewis has stated: "There is no evidence that hard water has any bad effect—on the contrary, the evidence is all the other way."

HARD v. SOFT WATER.—Tabulated results of examinations give no indication whatever that the hardness or softness of waters have anything to do with the prevalence or mortality from cancer, phthisis or enteric, similarly the character of water supplies in this country has nothing to do with the general death rate.—J. C. Thresh, B.M.J. ii./13,1058.

Magnesium Estimation. Render the water neutral to Methyl Orange and treat with Potassium Oxalate in slight excess of the amount equivalent to the Calcium present, and then with a measured excess of a mixture of standard alkali hydroxide and carbonate solutions. The liquid is then made up to definite volume and filtered, an aliquot part of the filtrate treated with an amount of Calcium Chloride equivalent to the excess of Potassium Oxalate used, and the excess of alkali titrated.—Abst. Ann. Rep. Chem. Soc. 1919 (Vol. XV.), p. 141.

Interpretation of Results.

Before a final judgment can be delivered upon any water there have to be taken into consideration (1) its geological history, (2) the rainfall before and after collection, (3) the method of storage and distribution, (4) the surface drainage, and (5) a bacterial examination. A water which chemically is organically pure may be bacterially contaminated, and on the other hand a bacterially pure water may be chemically dangerous or suspicious.—Purvis, P.J. ii./10,149.

IODINE IN NATURAL WATERS.

The Iodine content in drinking waters has interested us during the past year from the following aspects:—

- (1) The devising of a simple **process for determining the minute amounts** of the element.
- (2) The possible association of a diminished natural Iodine content with **endemicity of goitre**.
- (3) The possibility of the natural Iodine in water being **eliminated as the result of Chlorination treatment**, e.g., in the Metropolitan Water Board's supplies.
- (4) Work in other countries on the subject.

The 'goitre problem' is not new, though it has recently been attracting attention. It is of interest to recall that as far back as 1851, M. Marchand (a Pharmacien of Fécamp) together with M. Chatin, discussed the association of endemicity of goitre with the Iodine content of rain, river and sea-water, air and soil.

The estimation is surrounded with a number of technical difficulties and it was necessary to verify the accuracy of the methods of previous workers. The process we have devised has, we think many advantages.

1. Estimation of Iodine in Water.

The following process was tried at the outset:—

Modified Hunter's Method.

In a survey of water supplies in Kansas, U.S.A., H. W. Brubaker, H. S. Van Blarcom and N. H. Walker (Jl. Am. Chem. Soc., June '26, p. 1502) used Hunter's Method, as employed for Thyroid estimations. This consists in oxidising the Iodide to Iodate by boiling with Sodium Hypochlorite Solution acidified with Phosphoric Acid and continuing boiling until all free Chlorine is driven off. The solution is then cooled and Potassium Iodide added, from which the Iodic Acid formed liberates Iodine. The Iodine is titrated with Standard Sodium Thiosulphate Solution, using Starch Indicator.

The following reagents are required: (1) Sodium Hypochlorite Solution, of which the Chlorine content is roughly known; (2) Phosphoric Acid, made by diluting the 85% acid with an equal volume of water; (3) 1% Potassium Iodide Solution; (4) Standard Potassium Iodate Solution for standardising the Thiosulphate Solution; (5) Standard Sodium Thiosulphate Solution of strength 0.00474 N or N/211 (1 Cc.=0.1 mgr. Iodine in the sample).

In this method six times as much Iodine is titrated as was originally present in the sample, making it possible, it is suggested, to use smaller samples, thus obviating the evaporation of large volumes of water, 1 to 2 litres, evaporated to about 200 Cc., being sufficient. For each determination 50 Cc. Solution of Chlorinated Soda, U.S., should be used and 40 to 60 Cc. of the Phosphoric Acid Dilution.

Phosphoric Acid gives more reliable results than Sulphuric Acid.

The authors quoted speak well of the method, but we found it unsatisfactory for the minute amounts of Iodine present in 1 to 2 litres. The Thiosulphate Solution is too strong.

Process of Isabella Leitch and J. M. Henderson (Biochem. Jl., '26, 20, 1003). (A modification of Von Fellenberg's Method as described by Veil and Sturm, Deut. Arch. Klin. Med., 147, 166, 1925; Biochem Z. 139, 371; 142, 246; and Kendall's process. —J. Biol. Chem. 19, 251; 43, 149).

A convenient quantity of the water—we employed 5 litres—with the addition of 1 Gm. of Potassium Hydroxide (Iodine-free), is evaporated to dryness and the residue heated in a 6 cm. nickel crucible until bubbling ceases. The crucible is then further heated in a furnace until the ash is dark grey. The crucible must not glow. It is then cooled and the ash is moistened with water and again heated in the furnace (about 10 minutes).

After cooling, the ash is extracted with water and the solution filtered through a No. 44 Whatman Filter Paper. The filtrate is set aside.

The filter paper is returned to the crucible and heated in the furnace until a clean ash is obtained. When cool, the filtrate is returned to the crucible and evaporated to dryness, and finally heated in the furnace for 1 minute, then cooled and 3 Cc. of water added.

The thick solution is gently evaporated until a skin forms on the surface. The crucible is then cooled and the ash extracted three times with 95% Alcohol and filtered through Whatman Paper. The filtrate is evaporated to dryness and the residue gently glowed for a few seconds. When cool, the contents are dissolved in water and transferred to a 50 Cc. flask. Two drops of Methyl Orange Solution 0.05% are added, and the solution made just acid with 2N H_2SO_4 and about 1 Cc. Bromine Water added.

The solution is boiled down to 1 or 2 Cc. and cooled. Two drops of Potassium Iodide Solution (a small crystal in 20 Cc.) and two drops of Starch Indicator are added, and the solution titrated with N/500 Thiosulphate, using a serum pipette (0.1 Cc. graduated in 1/1000 Cc.).

If due precautions have been taken, the end-point is quite definite. Calculation:—

Titration figure \times Iodine equivalent of Thio.

6

gives the amount of Iodine in the sample.

(E. C. Kendall considers his method applicable to quantities of Iodine ranging from 0.005 to 5 mgr., which is obviously of little use for the quantities under consideration.)

The quantity of iodine in waters is usually expressed in terms of y per litre of water, where 0.001 mgr., i.e., 1/1,000,000 Gm., or 0.000001 Gm., equals 1.0 y , a factor which has been used throughout the work.

Orr, Godden and Dundas drew attention to two possible sources of error in the method (the analyses are detailed later).

(1) Where the water on making alkaline and evaporating gives a big precipitate of Calcium Carbonate or of salts, it is sometimes difficult to ensure complete extraction of the Potassium Iodide with Alcohol. It is desirable, therefore, after the first ashing, to extract the residue with about 10 Cc. of hot

water, repeating this extraction twice. The estimation of Iodine in the residue and the aqueous extract is then proceeded with separately in the manner described.

Thus, Canterbury hard water (*postea*) gave by the usual method 0.25 γ per litre and by the aqueous extraction method 4.32 γ per litre. Similarly, Cambridge water gave (*postea*) 0.08 and 0.8 γ per litre respectively.

(2) In the case of an acid mineral water with a high Iodine content there may be a marked loss of Iodine between the times of collection and analysis, unless sufficient Potassium Hydroxide is added to the water to make it alkaline at the time when the sample is taken. Thus, without this precaution Chadnor Villa (Cheltenham) water gave 285 γ per litre and with this precaution 930 γ per litre.—Jl. Hygiene, Jan. 25, 1928.

Our own criticism of these methods is that they are lengthy and require great care in conducting.

Under ideal conditions, and with practice, no doubt they will work, but we were in search of a simpler process.

Permanganate Method.

Impressed with the extreme minuteness of the quantities of Iodine under consideration—of the order of a few millionth parts of a gramme per litre—we decided to evaporate much larger volumes than those used by others. We examined 25-litre quantities of numerous waters from different parts of the country.

The specimens were rendered alkaline by addition of Potassium Hydroxide, and on reaching a suitable volume, *e.g.*, 20 Ce., the liquid, together with all the solids which had deposited, was transferred to a separator, 1 Ce. of 5% Potassium Permanganate Solution was added and the liquid acidified with Sulphuric Acid and shaken out with Chloroform 5 Ce. The Chloroform layer was removed into tubes $\frac{1}{2}$ inch in diameter, allowed to clarify and compared with a series of Standards containing, *e.g.*, 0.05, 0.075, 0.1, 0.125 mgr. of Iodine, each in 5 Ce. Chloroform.

Dividing the resulting figure by 25, the content per litre is found. The contents in the series just referred to indicate respectively 2 γ , 3 γ , 4 γ , and 5 γ .

The method was good up to a point, but during the investigation it was dropped in favour of the following:—

Sodium Nitrite Process.

In this method 10 or 25 litres (the latter amount in preference) are rendered alkaline with Potassium Hydroxide and reduced to dryness. The residue is gently calcined, powdered, and *extracted with 95% Alcohol*. The Alcoholic liquor is evaporated to dryness and this residue also gently incinerated. (As a practical point, those having to work with the process will find it useful to know that by actual comparison we found that strong red heating, as distinct from gentle incinerating, made no appreciable difference—but reasonable heating is to be preferred.) The residue is then dissolved in 20 Ce. of water and transferred to a separator, 1 Ce. of dilute Hydrochloric Acid or *q.s.* added, then 5 Ce. of Petroleum Ether (in preference to Chloroform), and 1 or 2 drops of 10% Sodium Nitrite Solution and *shaken thoroughly* (use the *smallest* amount requisite to throw out the Iodine: avoid excess). Draw off the

pink Petroleum-Ether layer, after allowing to separate, into $\frac{1}{2}$ inch test-tubes, and match the tint with Standards, as previously mentioned.

The limit of delicacy of this test is about 18 γ , i.e., approx. $\frac{3}{4}$ γ per litre, on a 25-litre quantity.

By this process the author was able to demonstrate, May, 1929, approximately 4 γ per litre in the London main (West Middlesex Works) supply.

Experiments were made with a view to titrating the Iodine in Petroleum Ether Solution with Thiosulphate. For a small quantity of say 20 γ , Thiosulphate solution at least as dilute as N/500 is needed, because 20 γ are equivalent to 2/25 Cc. of that strength. Further, we have not found it possible to determine the end point accurately with Starch, on less than 500 γ . The project was abandoned. *The observation of the depth of pink colour as described is far more delicate.*

It may be mentioned that Von Fellenberg used a Potassium Nitrite and Sulphuric Acid method with Chloroform as solvent in respect of blood examinations.

Palladium Method.

The next process tried was a modification of M. Ad. Chatin's method (*Cf. Comptes Rend.*, xxxv., 46, 127 and 505). This involves evaporating 2 litres with alkali, calcining moderately and extracting with 94% Alcohol. The Alcoholic extractive is evaporated and calcined and the residue is taken up with water and estimated colorimetrically with Palladium (Palladous) Chloride solution, 1 in 2,000, acidified with Hydrochloric Acid.

The estimation is conducted in Nessler Glasses. A standard solution for comparison containing 1 γ per Cc. is used.

Hampton Water (taken direct from the Thames, strained, not filtered), we found by this means to contain approx. 4 γ per litre.

Oxford Water showed approx. 2 γ .

The Metropolitan Water Board's main supply at London showed approx. 4 γ per litre.

(*Note.*—Palladous Chloride has been employed in the past as a test for Coal Gas and Carbon Monoxide and was recently referred to for detecting escapes in the Holborn Gas Main explosions. It is important to remark that the Palladous Chloride we used for this Iodine investigation does *not* demonstrate these gases, hence possibility of confusion in our results on this score is ruled out. The best compound to employ for testing for Coal Gas is the Sodium-Palladous Chloride (Sodium Chloro-Palladite) in 1 in 1,000 solution. Gas passed into this gives a brownish-black coloration. Paper soaked in the solution may also be utilised).

Oxygen Incineration Method.

According to J. F. McClendon (*Jl. Am. Chem. Soc.*, 1928, 1093) drinking or sea-water **may contain too much organic matter** for Iodine analysis by such methods as Kendall's and Chatin's. A method is described in which the substance is ashed in an atmosphere of Oxygen in a Silica tube, the ash extracted with water or Absolute Alcohol and after evaporation taken up in 2 Cc. water. The solution is neutralised with Phosphoric Acid containing Sulphurous Acid, and Carbon Tetrachloride and Sodium Nitrite are added. The colour is then matched with a standard in a Bausch and Lomb Colorimeter. The method according to McClendon, seems to be accurate to 0.01–0.02 mgr.

2. Possible Association of Diminished Iodine Content With Endemic Goitre.

Whether or not the reason for goitre being endemic in certain parts of the world—parts of Lancashire, Derbyshire, Switzerland, the central districts of the U.S.A., and New Zealand—is attributable to the absence of Iodine in the drinking water is still unproven, though the subject is being vigorously followed up by health authorities. The opinions partly affirm and partly negative the theory. The ‘clinical’ treatment, by adding small quantities of Iodine to the domestic salt or by other means, is fully discussed in Vol. I. of this Edition, pp. 517, 714, 715, 775, 918, 1060, and 1063, to which reference should be made.

The Rowett Research Institute (Aberdeen) workers’ investigations have already been referred to. We take the following from the paper ‘Iodine in Drinking Waters,’ by J. B. Orr, W. Godden and J. M. Dundas (Jl. Hygiene, Jan. 25, ’28), previously mentioned. :—

Examinations by von Fellenberg in Switzerland (1923-4) and by McClendon and Hathaway (1924) in the U.S.A. have shown that in those countries drinking water in goitre areas contains less Iodine than in goitre-free areas. Results show that in this country (Gt. Britain) there is no correlation between the presence of goitre and a low Iodine content in drinking water. It is true that the lowest figure (Swindon) is for water from a goitrous area, but the next one (Aberdeen) is not. The figures for Cumberland, Derbyshire, both goitrous areas, are not low.

(We deal with recent results in New Zealand later—the data obtained there contradict the opinions given here.)

TABLE I.

<i>Samples of Town Supplies.</i> <i>Iodine γ per litre.</i>				<i>Samples from Goitre Areas.</i> <i>Iodine γ per litre.</i>			
London (Thames—Hammersmith)	4	20		Cumberland (1)	..	1	30
„ (Kent Chalk—Deptford				(2)	..	3	90
„ Garden Well)	..	0	65	(3)	..	2	45
Manchester	..	2	00	Derbyshire (1)	..	1	66
Liverpool	..	2	00	(2)	..	2	10
Leeds	..	2	55	(3)	..	1	87
Shepton Mallett	..	2	58	(4)	..	1	84
Canterbury	..	2	14	(5)	..	1	40
Cambridge	..	0	80				
Swindon	..	0	52				
Edinburgh	..	1	70				
Glasgow	..	1	90				
Aberdeen	..	0	63				

Effect of Treatment of Water Supplies.—It has been suggested by Durham (Jl. Hygiene, 1921, 19, 394) in this country that goitre has increased in Hereford since the introduction of a pure water supply by the laying down of filter beds in 1911. Pennink (1924) in Holland also suggests that the increased goitre incidence in that country during recent years may be due to the purification of water, Iodine being lost in the process of filtration by adsorption in the filter bed. This has now been shown by Heymann (1925) not to be true for Amsterdam water, the Iodine content of the water being the same before and after filtration.

The examination of Aberdeen water, sampled direct at the intake and at the various stages in the process of purification, and of Edinburgh water before and after filtration, show that in each case there is a small loss of Iodine. The loss is, however, too small to be of any significance, and in the case of Aberdeen water is less than the fluctuations in Iodine content which occur naturally from time to time.

A much larger loss of Iodine was found to take place in the process of softening a chalk water by Clark's process (addition of Lime). Canterbury water before treatment was found to contain 4.32 γ per litre, and after softening only 2.14 γ per litre.

TABLE II.

EFFECT OF FILTRATION.

Iodine γ per litre.

Aberdeen Water Supply	..	Direct from River	0.63
"	"	"	After settling	..	0.58
"	"	"	"	and aeration and filtration	0.59
"	"	"	"	"	0.57
Edinburgh Water Supply	..	"	Before filtration	..	1.49
"	"	"	After	"	1.20
Canterbury Water Supply		Hard	4.32
"	"	Softened	2.14

Mineral Waters.—The Spa waters from Harrogate and Cheltenham were also analysed. In every case the Iodine was found to be much higher than that of ordinary drinking waters, and in some cases it is so high that it appears likely that the medicinal effect of the water may be partly due to the Iodine. The following table shows the amounts found. Strathpeffer Sulphur Spring was also examined and found to contain only 3.2 γ per litre, the lowest figure found for a mineral water.

TABLE III.

Spa Waters.

<i>Harrogate Waters.</i>	<i>Iodine γ per litre.</i>	<i>Cheltenham Waters.</i>	<i>Iodine γ per litre.</i>
Pure Chalybeate	.. 15.6	Fieldholme	.. 28.2
Chloride of Iron Well	.. 303.0	Chadnor Villa	.. 930.0
Harlow Water	.. 11.4	Pitville	.. 120.8
Well No. 36	.. 197.0	Lansdowne	.. 1058.0
Old Sulphur	.. 610.0		
Magnesia Well	.. 71.5		

Results of our Analyses of Water from Goitrous Areas in this Country.

We have examined three samples of such water:—

Buxton (Derbyshire) showed	2 γ per litre
Sussex (a surface Spring) ..	3 γ ..
Aberdeen ..	1.5 to 2 γ ..

Waters from other Parts of Gt. Britain.

We have found as follows:—

London (West Midx.) Main, Chlorinated	approx.	4 γ per litre
Hampton (Direct from the Thames) ..	"	4 γ ..
Distilled London Water ..	"	2 to 3 γ ..
Oxford ..	"	2 γ ..
Canterbury ..	"	3.3 γ ..
Llandudno ..	"	4 γ ..
Manchester ..	"	2 γ ..
Norwich ..	"	5.5 γ ..
Plymouth ..	"	2 γ ..

Sea Water.

It seemed of importance to include an examination of sea-water in our investigation. The Iodine figures stated by others in the past show an extraordinary divergence in findings:—

AMOUNT IN γ PER LITRE.	REFERENCE.	NOTES.
2000	E. Sonstadt, Chem. News, 25, 1872, pp. 196, 231, 241; 74, 1896, p. 316	Present as Iodate.
2380	A. Gautier, Comptes Rend., 128, 1899, p. 1069; 129, 1899, p. 9.	Largest amount reported. In the Mediterranean was only present in the organic matter separated by filtration, except at greater depths than 800 metres.
20	J. Koettstorfer, Z. Anal. Chem., 71, 1878, p. 305	Agreeing with Carmalt-Jones, L. i./29, 110.
50	L. W. Winkler, Z. Angew. Chem., 29, Pt. I., 1916, p. 205	
3.57	Thorpe, Dictionary of Applied Chemistry, 1912	In the Atlantic (Stanford).
920—944	U.S.D. 1926	

A further reference is in a paper by Von Fellenberg, 'The Occurrence of Iodine in Nature,' Part IV., Biochemische Zeitsch., 1924, 152, pp. 132-134, which refers to the escape of Iodine from sea-water and its loss from same after standing.

We do not find the opinion that the element is in the form of Calcium Iodate substantiated. Working with controls, there was no difficulty in reducing a solution of this salt, e.g., 1,000 γ per litre or less, with Sulphurous Acid, and obtaining results agreeing with theory by our Sodium Nitrite process.

Operating on sea-water under identical conditions results were practically nil.

The amount present according to our examinations (June, 1929) of the water in the English Channel is about 20 γ per litre. We incline to the view that it is in part in organic combination.

3. Possibility of Chlorination Resulting in Iodine Elimination— and other Results of our Analyses.

Chlorination as employed by the Metropolitan Water Board involves dispersing liquid chlorine in the water in the proportion of 150 lbs. per 30,000,000 gallons, i.e., 0.5 part per million. After filtration, 0.25 part per million is thought to be present. In winter 50 lbs. is used instead of 150 lbs.

The West Middlesex Water Works water, delivered at the mains in the author's Laboratory in London showed, as already mentioned, approx. 4 γ per litre.

Note the 4.2 γ per litre in Table I, as found by the Rowett Research Institute. This refers to water as supplied to the consumer, i.e., after Chlorination, etc., treatment.

The *Hampton water*, i.e., the same water taken direct from the river just prior to Chlorination showed an almost identical amount, viz., 4 γ per litre as already stated. This is, of course, a result of great importance.

At a somewhat later period, viz., at the end of July, 1929, *after* a remarkably **prolonged drought** in S.E. England, 50 litres of the London Main water and 50 litres of Hampton water were examined. The main supply showed **24 γ p. litre** and the (unfiltered) Hampton sample **40 γ** —a notable increase. Scientifically it will be important to confirm this on a future occasion. The Iodine in Petroleum Ether was shown to Sir A. C. Houston.

The investigation was conducted *again* in Aug. '29 after heavy rainfalls on 25 litres of each. On this occasion the waters had returned to more 'usual' content, namely 4 γ in the 'Main' and 8 γ in the untreated water.

It seemed of interest to examine also a sample of water from higher up the Thames, unchlorinated, and at a spot relatively free from drainage, etc., intake. A sample of water from the river at *Oxford* was therefore collected and showed, as already mentioned, approx. 2 γ . This water was taken at King's Weir, near to the intake of the water which is supplied to the City of Oxford.

Further, it seemed desirable to compare water from an *artesian boring* in London. Messrs. Idris, Ltd., supplied us with water of this description; it was found to contain 1 to 1½ γ per litre.

4. Results Obtained Abroad.

Iodine in Relation to Goitre (New Zealand).—The amount of Iodine in the normal thyroid is about 0.1% of dried substance, and it is estimated that 10 mgr. of Iodine must be ingested per annum to maintain this concentration, and if the essential amount of Iodine is not present in natural food it must be deliberately added. The amounts actually present both in soils and in food are exceedingly minute. The ingestion of the necessary 10 mgr. of Iodine, or 10,000 γ , involves an extra intake of about 200 γ per week, or 30 γ a day. It is evident that if the soil is deficient in Iodine then the thyroids of the animals living in the district, unless they are able to adapt themselves, will show symptoms of disease. **Deficiency of Iodine in soil is found in many districts in New Zealand where goitre is highly prevalent.** The only supposed cause of endemic goitre which Hercus could find applicable in New Zealand (from an examination of 90,000 school children from 33 districts) is deficiency of Iodine.

Experiments on the Iodine content of foodstuffs raised on Iodine-poor and Iodine-rich soils respectively, gave the following results (γ per kilo):

Grass, 47 as against 64; Lettuce, 12 as against 24; Beef, 9.5 as against 16; Eggs, 56 as against 137. Hence the essential Iodine is normally derived from the soil, though in exceptional cases a deficiency may be made good by an Iodine-rich water (Hercus found that only in one district did the drinking water make up the Iodine deficiency, and in that instance the water was contaminated with sea-water). In Taranaki, with goitre incidence of 7%, the Iodine intake per person daily was 35 γ ; in Canterbury with goitre incidence of 60% the intake was 20 γ ; i.e., a difference

of 15 γ daily turns a low goitre incidence into a high one. Iodine deficiency is apparently the cause of New Zealand goitre.

The obvious prophylactic treatment is addition of Iodine to the diet; this is not new, but what is new is recognition of the minute amounts of Iodine required. The Iodised Salt sanctioned by the New Zealand Government contains 4 parts per million Potassium Iodide. The normal consumption of salt being 6 Gm. per diem (6 million γ), this gives a daily intake of 24 γ Potassium Iodide, and has been proved adequate and perfectly safe from risk.—D. W. Carmalt-Jones, quoting the work of C. E. Hercus, E. Baker, A. M. Drennan, C. L. Carter, W. N. Benson, and others.—B.M.J. ii. /28,712; L. i./29,110,164.

Wool Growth in Sheep in Australia.—Iodine as a factor is being studied by the Rowett Research Institute, with the aid of London rats sent out for the purpose—and from the aspect of general nutritional work.

Nebraska, U.S.A. The amounts of Iodine in water, etc., in the centre of the United States are notoriously minute. We observe that W. H. Adolph and F. J. Prochaska (J.I.A.M.A., June 29, 1929), working on 100 litre batches, were able to detect quantities of the calibre of parts per **100 thousand million** (i.e. per 100 billion, as understood in U.S.A.), using a colorimeter. These amounts are of the order of **10 times less** than those with which we are conversant in Gt. Britain. It is stated that Nebraska water supplies contain sufficient Iodine for the maintenance of thyroid equilibrium, and that simple goitre is not prevalent.

In Holland much work has been conducted on Iodine in water by Heymann, Penninck and others. The papers (printed in '*Water en Gas*,' Amalia van Soemsstraat, 2—8, Den Haag) have not apparently been abstracted in English publications.

Heymann ('*Water en Gas*,' 1925, Vol. 9, p. 39) maintains that the Iodine content is unaltered by filtration, but there is no mention of Chlorination of the supply he had under investigation. In reality, the dune water is so pure that Chlorination is unnecessary.

In a communication to the writer (Feb., 1929), Dr. Heymann says:—

'At Weesperkarspel, our river-water works, the water is Chlorinated in one of the settling basins before double filtration.

Technical difficulties in this case made Chlorination of the filtered water almost impossible.

Chlorination before filtration has the advantage that the assimilable organic matter, which is formed by the Chlorination, is oxidised in the filters. This diminishes the chance of after-growth and bad taste of the water delivered by the pumping station.'

According to his findings:—

(1) The water of the dunes owes its Iodine content, roughly, to the influence of the sea.

(2) The two principal Iodine sources of dune-water are the shell material which is present in the neighbourhood of the dunes, and vegetation.

(3) The vegetation is of more importance in this matter than the shell material.

(4) Deep water is richer in Iodine content than surface water.

The paper gives much detail concerning both inorganic and organically combined Iodine.

Iodine in the Air.—*Inter alia*, Heymann mentions that he has frequently estimated this by suction through a concentrated

Potassium Hydroxide solution at his Laboratory, which is 6 kilometres from the sea. He found:—

DATE.	DIRECTION OF WIND.	ATMOSPHERIC CONDITIONS.	IODINE γ 'S PER M ³ .
Sept. 4, 1924	East	Dry	0.5
„ 8-10 „	W.S.W. to W.	Rainy	1.0
„ 17 „	W.S.W.	Stormy	0.2
November, 1924			1.6
December, „	S.E		+ 0.3

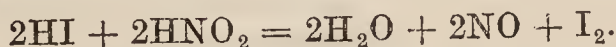
Broadly, the west winds show an increase.

(Chatin also did a large amount of work on the estimation of Iodine in the air, see *Comptes Rend.*, XXXV., *et seq.*)

Von Fellenberg has observed that natural water supplies (especially hard water) gradually lose their Iodine on exposure to air. The reason of this is as follows:—Hydriodic Acid is a relatively weak acid which can even be split off by Carbon Dioxide, a constituent of all waters:—



Further reactions follow from nitrites in the water. HNO_2 may be formed by the activity of CO_2 upon nitrites and this HNO_2 may react thus:—



In the same journal for May 30, 1927, is a further paper on the Iodine content of dune and rain water.

The Iodine content of rain water in the dune district near Haarlem amounts on an average to 3 γ per litre. Of this only about half finds its way into the dune water in the soil.

The effect of Chlorination (0.6 mgr. Chlorine per litre employed), upon removal of organic material, is dealt with in further papers by Heymann ('*Water en Gas*,' 9 and 23, March, 1928).

In Germany we understand, Chlorination is much in vogue.

In Finland E. Adlercreutz of Helsingfors has been concerned with the relation of the Iodine content of water to goitre. The waters in that country appear to be relatively weak in Iodine. Adlercreutz makes a figure of 40 parts per hundred thousand millions as a criterion of waters above or below which may be considered rich or poor in Iodine. 40 parts per hundred thousand millions is equivalent to 0.4 γ per litre.

In a review in the B.M.J. (July 13, '29, p. 62) it is thought doubtful whether this worker has succeeded in establishing association between goitrous and non-goitrous areas with regard to Iodine content of water, and he is criticised for assuming that the Iodine content of water is a fair reflection of the Iodine content in soil, air, and food produce. Our rejoinder would be that we can see no valid reason why a low content in food produce should be associated with a high content in water, and conversely why a low content in water should be associated with a high content in food produce. We know by analogy, in respect of other chemicals (Lime, Magnesia, etc.), that plants take up these substances with avidity, if they happen to be present in excess, but *we see no reason why a plant should, so to speak, go out of its way to assimilate Iodine in excess of its requirements from soil poor in the element, for the benefit of mankind*. Application of fertilisers containing Iodine considerably increases the Iodine in plants.—B.C.A., '26,667.

Chlorination of Water.

A survey of the known methods of sterilisation of water shows that no method so economical or expeditious as Chlorination exists.

Sir A. C. Houston first used an alkaline Hypochlorite in 1905 at Lincoln in a typhoid epidemic. The method is in use in many parts. In Bogotá (Colombia) typhoid diminished on the introduction of the process. It is done either after or before filtration. In some cases a large excess of Chlorine is added to destroy algæ as well as bacteria, the excess being removed by means of SO_2 . Chlorine produced by electrolysis of sea-water is used in some parts instead of Chlorine cylinders. In France, Eau de Javelle is employed. In the Bunau-Varilla method in use at Rheims the amount of Chlorine used is small and the good results do not seem capable of explanation on the basis of chemical interaction.—See T. H. Bishop, L. i/29, 371; also E. W. Wade, JI. R.A.M.C., Oct. '28.

Liquid Chlorine has many advantages over the use of 'Bleach'—the 100% purity of the sterilising agent, elimination of nearly all labour costs, and less likelihood of complaints as to taste, as it permits of more accurate dosage and better distribution of the Chlorine in the water. In some cases the Chlorine is dissolved in water through a pulsating meter before mixing; in others it enters the water through a diffusion plate of Carborundum sponge.—'Chlorination of Water.'—J. Rice (1918).

Nesfield found 0.125 Gm. Chlorine per litre (125 per million) in water teeming with *B. Typhosus*, *B. Coli*, etc., sufficient to sterilise it in 5 minutes. One part per million acting 15 minutes will kill *Cholera vibrio* in it.—L. ii./10, 1213.

Sterilisation by means of Chlorine in proportion of 1 in 500,000 with 30 minutes' contact. The gas made by acting on Potassium Chlorate with Conc. HCl.—both of which have the advantage of keeping indefinitely in any climate.—J. J. Harper Nelson, B.M.J. i./15, 789, 815. cf. also *Calx Chlorinata*, Vol. I., p. 45.

The addition to excessively polluted water of a quarter or a half part of Ammonia per million, prior to its exposure to Chlorine, increases the lethal action of the Chlorine on the organisms without deterioration of taste.—L. ii./24, 384.

The "Chlor-Sparklet" Apparatus enables the use of Chloramine (Cf. Vol. I., p. 51, *et seq.*) to be applied in effective doses to small quantities of water by an unskilled person.

The apparatus involves the preparation of Chlorine Water from a Chlorine Capsule and then adding an Ammoniacal Solution made from Tablets supplied.

Two Chloramines exist:

Mono-Chloramine, which is rapid in its action, but its protection against reinfection disappears after 24–48 hours.

Di-Chloramine is slower in its action (allowing 2 hours before using for drinking) but protects the water from reinfection for periods up to a week. Mono-Chloramine is prepared by using two tablets to each syphon full, whereas with Di-Chloramine only one tablet is required.

Chlorination may play a part in preventing the breeding activities of *Stegomyia fasciata* (*Aedes ægypti*), thus aiding the campaign against yellow fever. In countries bordering the Gulf of Mexico, where the water is filtered and chlorinated, yellow fever has been got under control, whereas on the West Coast of Africa where this is not done to any extent, cases still occur.—Bunau-Varilla, per Trans. Roy. Soc. Trop. Med., Jan. 30/29, 395

Succin Chlorimide suggested as acting promptly and being non-toxic for War Service in U.S.A. Bleaching Powder said to be too erratic.—L.i./29,352. A plant was put down at Ottawa in which Chloramine was used. Although slightly more expensive, it is stated to have the advantage of preventing after-growth, which is a serious problem on the Continent.

Further Methods of Sterilisation.

Copper was suggested some years ago by H. Kraemer as a domestic measure for ridding water from *B. Coli* and *B. Typhosus*. His recommendation was to immerse a strip of Copper Foil in the water, e.g., a piece $3\frac{1}{2}$ inches square being used in a quart of water for six hours.

We recently conducted (1929) a number of experiments on the possible bactericidal action of the metal used in this manner, but we did not find the contention substantiated. We fear, therefore, that Krämer's recommendations cannot be regarded as really trustworthy.

Cushny, referring no doubt to Kraemer's work, relates that certain organisms in water, stored in a copper vessel, are affected and killed by copper in solutions so dilute that the metal is not detected chemically.—J. Wilson Dougal, P.J. i./28,216.

Ozone has been utilised abroad, but is far more expensive than Chlorine.

Ultra-Violet Light (the Cooper Hewitt Apparatus) is most effective, with a flow of 600 cubic metres per 24 hours, and a consumption of less than 26 Watts per cubic metre it reduces a bacterial count of 500 to 1,000 *B. Coli* per litre, and total germs of 20 to 260 per litre, to nil and practically nil in each case. It also destroys spores.

Conclusions.

(1) We have shown by a somewhat prolonged investigation in our Laboratory that the Nitrite Method devised by the author is suitable for estimating minute quantities of Iodine. It has the advantage of demonstrating the Iodine *as such* in Petroleum-Ether solution. The process is far more delicate than all the other methods, particularly if a volume of 25 litres be examined.

(2) So far as Great Britain is concerned, though the differences are small and not uniform, we certainly find a diminished Iodine content in the water of districts which are known to be goitrous. The New Zealand work lends support to the association of the Iodine factor. It is true that authorities, both at home and in New Zealand, lay stress rather upon the Iodine content in the soil and foodstuffs, but it is reasonable to maintain that Iodine deficiency in water will run parallel with a lessened content in the soil and food. The average man consumes at least a quart of water a day in some form or other. This quantity is, in fact, essential to health. Human blood contains 80% water.

(3) We have shown that the Iodine content of the water of the Metropolitan Water Board is *not* diminished by the Chlorination treatment. We have demonstrated its presence in amount comparable with that contained in the water just prior to Chlorination. It is satisfactory to know that the town-dweller is not being deprived of his natural Iodine as a result of a purification process of vast importance and enormous utility to the welfare of the community.

WATER STERILISATION FOR ARMY USE.

Horrocks's Water Testing Method is used to determine the amount of Bleaching Powder required to sterilise an army water-cart full.

The method uses Zinc Iodide or Potassium Iodide and Starch Solution as reagent.—Compare Field Sanitation by Moor & Cooper (Bailliere, Tindall and Cox).

The test automatically adjusts the strength of the purifier to be used, to the particular water to be treated. The Horrocks's Test Case contains 6 white enamelled tumblers (170 Cc.) and 1 black one (250 Cc.). Bleaching Powder—a levelled scoopful of about 2 grams—is rubbed fine and dissolved in the black tumbler filled to the inside mark. The white tumblers are filled with the water to be tested. One drop (1/15 Cc.) of Bleaching Powder solution is added to No. 1, two drops to No. 2, up to 6 drops in No. 6. These are stirred and left for twenty minutes, when about 6 drops of a stock solution of Potassium Iodide and Starch, are added to each. A blue colour will indicate that after all organic matter has been destroyed, an excess of available Chlorine remains, whereby Iodine is liberated with the formation of the blue Iodide of Starch. The number of the first mug of the series which shows a definite colour, gives the number of scoops of the Bleaching Powder required to sterilise the contents of one water-cart (110 gallons approx.). The powder should be dissolved before adding it to the water-cart, and contact for one hour should be allowed, before the water is issued to the troops.

Alum Box in the Army water filtering cart contains a mixture of Alum 75% and dry Sodium Carbonate 25%. By the action of the water Alum Hydroxide is formed and deposited on the filter cloth, the jelly-like mass-formed imitating the natural zoogloea layer of a sand filter bed.

POISONED WATER.

A set of Tests for examination of **Wells for Troops on the March**, including examination for **Cyanides**, **Alkaloids**, *e.g.*, Strychnine (using Bismuth Potassium-Iodide and Phosphomolybdic Acid), **Arsenic** (using Zinc, HCl and Mercuric Chloride spot on filter paper), **Mercury** (using Copper Foil and HCl), **Copper Salts** (using Hæmatoxylin Solution which turns a deep blue with Copper and Iron Salts). Eliminate the latter by adding a few drops of HCl and then a few drops of freshly made Potassium Ferrocyanide Solution. If the pp. be maroon coloured no iron but much copper is present. If both copper and iron be present, the maroon pp. of copper will be obscured. In this case insert the polished blade of a pocket knife in the water with a few drops of HCl.—and note deposit. The water if necessary may be concentrated.—John Parry, Kimberley, C.D., Oct. 23/15, 554.

The **Army Sanitary Committee** give the following scheme for detecting Poisons :—

(1) **Biological Test.**—If possible note effect on Fish.

(2) **Chemical Tests.**—Add Sodium Sulphide Solution, *q.s.* *Brown* colour indicates probable presence of a metal (but the absence of a colour does not indicate absence of Arsenic).

Add Hydrochloric Acid- *q.s.*—

(a) If the colour remains black or brown, **Lead, Copper or Mercury** is present.

(b) If canary yellow colour forms **Arsenic** is present. (Ignore slight milkiness of Sulphur).

Confirm by conducting a 'Marsh' with a small test-tube and glass jet, allowing the lit hydrogen flame to impinge on a porcelain plate. Black stain insoluble in dilute Hydrochloric Acid indicates Arsenic or Antimony.

For **Cyanide**. Add Caustic Soda solution and a few drops of Ferrous Sulphate solution. Boil thoroughly. Add Hydrochloric Acid, *q.s.* Blue colour indicates Cyanide especially on standing 30 minutes.

DISTILLED WATER.

Bacteriological Examination.

Some years ago the opinion was expressed that saline fever occurring after injection of Salvarsan was due to dead bacteria in the saline solution used as solvent of the arsenical compound—the effect was thought to be attributable to protein shock.

Donald's Method of counting Bacteria in water includes the dead bacteria, whilst the usual cultural methods eliminate them. Extraordinary differences are recorded. A water, for example, grown on Agar two days at 37° C. showed no organisms. On gelatin at 18 to 22° C. 10 to 14 days showed 160—300,000 per Cc., whilst by Donald's method there were 1,500,000 per Cc.

Drops of the water from special capillary pipettes are used. Bacteria contained in the water are counted by evaporating and staining on micro-slides. By the method it was shown that Distilled Water kept for three weeks may develop as many as 15,000,000 of bacteria per Cc.—*L.i./13,1447.*

Tap water always, and about 50% of all distilled waters, produces a rise of temperature when injected intravenously into rabbits. This fever is due to a bactericidal product formed by a specific bacterium which contaminates the water.—*F. B. Siebert and H. G. Wells, Jl. Pharm. Experim. Therap. Mar. 24/154.*

Experiments with Distilled Water.

We made an investigation to determine to what extent bacteria may increase in Distilled Water on standing.

500 Cc. of fresh Distilled Water were exposed in a flask and counts made in the usual manner periodically. Examination at the commencement showed *the water to be sterile.*

After 3 days there were 111 organisms per Cc. capable of growth on gelatine [at 18° C]

„ 10	„ „	52,000	„	„	„	„	„
„ 15	„ „	3,800,000	„	„	„	„	„

At this time there was only one organism per 2 Cc. capable of growth on Nutrient Agar at 37° C.

These results show the remarkable contamination in Distilled Water which may occur by air organisms. Whilst demonstrating the importance of fresh Distilled Water, the relative absence of pathogenic organisms is also of interest.

Ordinary Chemical means failed to detect any difference in the Water either at the commencement or end of these experiments.

Distilled Water has been advised as a **Therapeutic Agent** injected in dose of 6 to 8 Cc., for syphilitic ulcers, the theory being that increased surface tension has a good deal to do with beneficial results of injections.

DRINKING WATERS.

Bacteriological Examination.

Collection of Sample.—The apparatus used for collecting the sample consists of a sterile bottle which can be opened below the surface of the water, —at any depth by aid of a suspending string. A bottle of capacity 500 Cc. can be used.

If from a water-supply, the water should be allowed to run at least half an hour before collecting; if from a reservoir or stream, surface water must be avoided by holding the bottle at least one foot below the surface.

It is important to know whether the water, *e.g.*, a well, has been recently disturbed by cleaning out or pumping, also to examine as quickly as possible after collection, particularly in hot weather. To prevent increase in number of bacteria it is customary to pack the bottle in ice for transmission by rail, &c.

Unless the water be packed in ice there is a chance that saprophytic organisms may multiply at the expense of organisms indicative of pollution.

Enumeration of Bacteria.—Agar and gelatin plates are prepared with varying quantities of the specimen, *e.g.*, 1·0, 0·1, 0·01 and 0·001 Cc. and incubated at their respective customary temperatures and the colonies counted. A very pure water might of necessity require 3 Cc. The easiest way to do this is to draw sector lines with a paraffin pencil through the petri dish, count one section, and multiply out to obtain the number of bacteria in the entire amount of water taken for examination. **Pakes' Discs** are employed in a similar manner. To obtain accurate results it is important to add the melted gelatin or agar medium to the specimen of water, and not the water to the medium. This procedure ensures better mixing.

The plates are examined daily (2 to 4 days' incubation should be sufficient), and if liquefying organisms are numerous (which suggest sewage pollution) the examination has often to be concluded in a shorter time than would be necessary where such are not present; if possible a week should be devoted to growth.

By cultivation on Gelatin at 22° C., we enumerate the bacteria present normally in the water, whilst the body temperature 37° C. will be more suitable for excremental organisms—derived from, or pathogenic to, the animal body.

As glucose media are very favourable to the growth of many of the yeast and fungi it is advisable also to prepare a plate culture using this medium. Yeast and fungi are therefore often not included in the count with the ordinary media owing to the non-favourable condition for their development.

It is no longer considered of great importance to count the number of organisms in water, but to determine presence of *B. Coli*, *B. Enteritidis Sporogenes* Klein, (*B. Welchii*), and *Streptococci*.—J. C. Tresh & J. F. Beale, B.M.J. i./25,514.

The next step is to conduct individual search for various sewage polluting organisms, *e.g.*, *B. coli communis*, *B. typhosus*,—especially the *B. coli* group *Vibrio cholerae*, *B. proteus*, Klein's *B. enteritidis sporogenes*, and *Streptococci*.

B. Coli Communis.

The entire problem turns on determining whether pollution with sewage has occurred, indicated usually by the presence of the *B. Coli* group of organisms. Acid and gas production in **MacConkey's Litmus Bile Salt Glucose Broth Medium** gives presumptive evidence of the presence of *B. Coli*, *B. Paratyphosus*, *B. Enteritidis*—but excluding *B. Typhosus* and the dysentery organisms. These latter produce acid formation only (without gas) in this medium.

Fill ordinary test tubes into which Durham's tubes are introduced, with the following special broth (bile salt broth)—Sodium Taurocholate 0·5, Glucose 0·5, Peptone 2 Gm., Water 100 Cc., with 10 Cc. of 18% Sterile Litmus Solution.

Another step is to employ the **MacConkey Medium** made with **lactose** instead of glucose—this forms a useful corroboration for *B. Coli*—this organism gives acid and gas whereas none of the others do so. In tabular form the matter may be stated as follows:—

	GLU- COSE.	LAC- TOSE.	MOTIL- ITY.	GELA- TIN.	LIT- MUS MILK. 3 DAYS.	IN- DOL.
<i>B. Coli Communis</i> ..	A.G	A.G.	+	—	A.C.	+
<i>B. Typhosus</i> ..	A.	—	+	—	A.	—
<i>B. Paratyphosus</i> ..	A.G.	—	+	—	Alk.*	—
<i>B. Enteritidis</i> (Gaertner) ..	A.G.	—	+	—	Alk.	—
<i>B. Dysent. (Shiga)</i> ..	A.	—	—	—	Alk.	—
<i>B. Dysent. (Flexner)</i> .	A.	—	—	—	Alk.	+
<i>B. Morgans No. 1</i> ..	A.G.	—	+	—	O	+

A = Acid. G. = Gas. C. = Clot. — under Gelatin means non-liquefaction. * *Vide* also Eyre Bact. Technique, for *B. Paratyphosus*, A. and B.

The data in question, together with the production of fluorescence in the colonies in **Rebipel Agar**. *Syn.* **MacConkey's Neutral Red Bile Salt Agar**—which has the composition :—

Agar and Peptone White	aa. 30 Gm.
Lactose	15 Gm.
Sodium Taurocholate	7½ Gm.
Tap Water	1500 Cc.
Solution of Neutral Red, 1%	7½ Cc.

Constitute the '**Flaginac**' Reaction which is typical of *B. coli*.

This word is made up to show the reactions on these media and is applied to organisms, *e.g.*, *B. Coli*, which will respond to all:—

fl : fluorescence in neutral red.

ag : acid and gas formation.

in : indol in peptone water.

ac : acid and clot in Litmus milk.

Neutral Red $C_{15}H_{16}N_4$ (*Syn.* Toluylene Red) is chemically Dimethyl-diamido-tolu-phenazine hydrochloride. It is readily soluble in alcohol and in ether.

The exact mode of procedure which we employ for the detection of Acid and Gas formation is as follows:—

Examination of 100 Cc. of the Water. Place 50 Cc. of **Triple Strength MacConkey's Broth Medium made with Glucose** into a 130 Cc. bottle (an ordinary strong green flint bottle is suitable), containing a small inverted test tube, rendered bubble free. The whole is then plugged with Sterilised Wool and sterilised on three succeeding days. This has to be made ready before receipt of the specimen. 100 Cc. of the sample to be examined is introduced with aseptic precautions.

The same procedure is gone through with the *Lactose* preparation. These are then incubated 24 hours.

Examination of 50 Cc. of the Water. Take 50 Cc. of **Double Strength MacConkey's Medium** made with Glucose and Lactose respectively and 50 Cc. of the specimen in a 100 Cc. bottle, and incubate as before.

Examination of 10 Cc. of the Water. Take 10 Cc. each of the Double Strength Media and 10 Cc. of the sample and proceed as above.

Subsequent to these results inoculate Neutral Red Bile Salt Agar Plates with loopfuls from the cultures in the bottles—using a 'spreader' made with a piece of glass rod $\frac{1}{8}$ inch diameter with a bent end about $1\frac{1}{2}$ inches long at right angles to the handle.

After incubating 24 hours pick out with a platinum loop Colonies resembling those of *B. Coli*, and inoculate Sloped Agar tubes, *thence* Peptone Water for the Rosindol Reaction and Indol Reaction—also Litmus Milk for the 'Acid and Curd,' and examine a fresh broth culture for motility.

The plate cultures are incubated further to observe fluorescence, if any.

Rosindol Reaction (Ehrlich's). *Syn.* Böhme's Indol Test.—To 10 Cc. of a 48 hour Peptone Water culture add 5 Cc. of the following solution :—

Paradimethyl-amido-benzaldehyde	1
Alcohol, 96%	95
Concentrated Hydrochloric Acid	20

and then 5 Cc. of Saturated Aqueous Potassium Persulphate Solution. Shake well. MacConkey says 1 Cc. of each solution is sufficient, and we have found so. Pink colour in a few minutes = +. In some cases the Persulphate need not be added. The pink colour is soluble in Amyl Alcohol—a little of which should be added, especially in doubtful cases. At least 48 hours growth should be allowed, in some cases 6 to 8 days are required.

Indol Reaction.—To 5 Cc. of the (6 or 7 days) Peptone Water culture add 1 Cc. of Concentrated Sulphuric Acid and then 1 Cc. of 0.02% Sodium Nitrite. Pink colour indicates Indol production (some organisms, *e.g.*, *Colera vibrio* do not require the Sodium Nitrite—hence the test may be

done in two stages). It may be necessary to incubate for 8 days or more before conducting the test.

Our own experience with these two reactions is disappointing—on the whole we think the Rosindol Reaction is the more conclusive (*cf.* also *B. Coli* in Urine).

The formation of Indol amongst the '*flaginac*' characters of *B. Coli* is the character most liable to be absent in *B. Coli* isolated from urine (and water). The Rosindol Test preferred.—A. R. Tankard.

The presence of Indol can be shown by production of a pink colour on paper impregnated with Oxalic Acid held in the mouth of the culture tube. The delicacy of the test is influenced by reaction of the medium.—J.C.S.A. i./25,1510.

Thresh gives the following as "decisive tests" for *B. Coli*: (1) Acid and Curd in Litmus Milk (2 and 3), Motility and Indol in Peptone Water. (4) Negative to Gram's stain. (5) Liquefaction with streak cultures on gelatin. (6) Fluorescence on Rebbipelagar (7, 8 and 9). Fermentation of Sucrose, Mannite and Dulcitol respectively.—(Examination of Water Supplies, 2nd Edition.)

A thorough investigation of the source and history of a water under examination is necessary,—this is more important than laboratory diagnosis. To ascertain the *origin* of the organism if found,—whether from sewage or other human source, cattle, cultivated lands, etc.

The presence of **Sulphur Bacteria**, *Beggiatoa alba*, which are readily identified, may be used for detecting sewage pollution, in place of a *B. Coli* count.—Prof. Davis Ellis, P.J. ii./26,308.

B. Typhosus.—In searching for this organism, it is the custom to accept the indirect bacteriological evidence obtained by the *coli-form* data, as sufficient for the purpose of condemning or passing a water for drinking purposes. Scheme of work for isolating *B. Typhosus*:—

- | | | | |
|----------------------------|---|--|---------------|
| 1. ISOLATION. | { | 1. Chemical precipitation—Schüder's or Ficker's process | |
| | | 2. Serum agglutination. | |
| | | 3. Solid Media { <table border="0" style="display: inline-table; vertical-align: middle;"> <tr> <td>Rebipel Agar.</td> </tr> <tr> <td>Glucose and Lactose Agars.</td> </tr> <tr> <td>Drigalski-Conradi Medium.</td> </tr> </table> | Rebipel Agar. |
| Rebipel Agar. | | | |
| Glucose and Lactose Agars. | | | |
| Drigalski-Conradi Medium. | | | |

IDENTIFICATION. {

Morphological and cultural characters, &c.
Specific Reactions : Pfeiffer's Agglutination Test.

Schüder's Process consists in adding to 2 litres of the water 20 Cc. of 7.75% Solution of Sodium Hyposulphite and 20 Cc. of 10% Lead Nitrate Solution. Plates are made from the precipitate containing the bacilli.

Flicker's Process.—Render 2 litres faintly alkaline with Soda and add 7 Cc. of 10% Ferrous Sulphate Solution. The precipitate is dissolved in 25% neutral Potassium Tartrate, and plates are prepared.

Serum Agglutination.—Add 1 Cc. of the sample to each of a number of broth tubes, and incubate at 37° C. three or four days. To those with sediment add a few drops of active anti-typhoid serum. Clumps are centrifuged, and the clear liquid drawn off. Emulsify deposit and prepare plates.

Solid Media.—**Drigalski-Conradi Medium** consists of a nutrient lactose-litmus agar containing 1% Nutrose, 1% (a Sodium Caseinate Compound), Peptone 0.5% Salt, 3% Agar, 1.5% Lactose, in a nutrient broth made with 750 Gm. Horse Flesh to the litre, also 13% of Kübel and Tiemann's Litmus Solution and a trace (0.001%) of Crystal Violet. After incubation typhoid colonies are blue, glassy like dew drops, Paratyphoid similar, and *B. Coli* are bright red and opaque.

Rapid method which may be utilised in search for *B. typhosus*—“Concentrate” at least two litres of the water by filtration through a Chamberland filter. Brush off the organisms from surface of candle into sterile vessel containing about 10 Cc. of sterile water and examine as previously directed.

Vibrio Cholerae.—To detect: inoculate peptone water, preferably in an Erlenmeyer flask with 100 Cc. of the water. Incubate and test for indol production and search for typical comma-shaped organisms, which are actively motile and decolourised by Gram's method. Test further with usual laboratory media, and also conduct serum agglutination test.

The above method somewhat modified used for cultivation. Identification by motility, Cholera Red Reaction, Nitroso Indol, Ehrlich's Rosindol Reaction. Flagella staining, and Agglutination Test.—L. i./13,1377.

B. Proteus.—The ordinary laboratory media and methods may be employed for the various types of *Proteus*.

Bacillus Enteritidis Sporogenes.—Add to a fresh milk tube 1 Cc. of the water or a small quantity of the 'concentrated' water. Heat to 80° C. for 20 minutes to kill off other organisms, excepting spores of the organism searched for (Kitasato's method): grow in Buchner's tube, i.e., in an atmosphere of nitrogen for 24 to 36 hours. If result be separation of milk, stringy curd, and excessive whey, test for pathogenicity on guinea-pig. The animal succumbs within 36 to 48 hours (if very virulent in 24). Post-mortem signs: bloody œdema at seat of inoculation, offensive odour, hair of animal easily detached. Films stained by Gram's method from œdema fluid show typical non-sporing organisms. To further test, a blood serum tube is inoculated from the œdema fluid and incubated under anærobic conditions. The medium is eventually liquefied by the organism, and films prepared from this show the typical sporing organism of Klein.

Streptococci.—Eyre (Bact. Technique), states the Streptococci are frequently termed 'microbes of indication,' as their presence is held to be evidence of pollution of water by material from the mammalian alimentary canal—thus constituting a danger signal. Glycerin Agar is a good medium for this organism. Agar plates may be brushed or prepared in the ordinary way, incubated at blood heat, and all discrete colonies examined by films or ordinary sub-cultures made on various laboratory media.

Leptospira Icterohæmorrhagiæ found in London Tap Water.—*cf.* pp. 442 and 610.

BACTERIOLOGICAL REPORTS ON WATERS.

If *B. Coli* form a considerable proportion of the total number of organisms present there is great reason to suspect sewage pollution of human or other animal origin.

The following is a brief résumé of the customary standards:

A water generally speaking containing B. Coli in 50 Cc. but not in less is quite good if the count of total bacteria and chemical analysis are good. See also filtered London Lea River Water, postea.

Wells, Shallow and Surface.—

If chemical results and surroundings are bad, even if *B. Coli* be absent from a large volume of the water, it should be condemned, and *per contra* if in a suspicious locality the bacteriological examination is bad the water ought to be condemned even though chemically it could be passed.—M. and R.

The **usually accepted standards** for a surface water are:—

B. Coli absent in 10 Cc.

Streptococci absent in 10 Cc.

B. Welchii absent in 100 Cc.

Total colonies at 37° C. = 50 per Cc.

“ “ “ 22° C. = 500 “ “

Wells, Ordinary or Medium Depth.—

Total Bacteria.—The Gelatin Count may show from 100 to 2,000 organisms per Cc. The presence of *B. Coli* in 10 Cc. would condemn the water.

Wells, Deep.—

Total Bacteria.—Should not exceed 100 bacteria per Cc. Artesian Wells and some springs may contain very small amounts, e.g., 5 or 10 organisms per 100 Cc.

Presence of *B. Coli* in 100 Cc. or less cannot be permitted.

Rivers.—Draw conclusions as under Wells (Shallow). Content varies enormously with season.

Total Bacteria.—The Gelatin count varies enormously. *B. Coli* in 10 Cc. would condemn.

Town Supplies (Filtered).—

Total Bacteria.—Should not show more than 100 Bacteria per Cc. —Muir and Ritchie.

London (Lea River filtered).—

Though *B. Coli* in one series of examinations was present in 93% of samples in 1 Cc. or less before filtering it was absent from 100 Cc. in 62% of samples after filtering, and therefore present in 38% of 100 Cc.—Sir A. C. Houston.

A well known authority on bacteriological examinations of water informs us that he would expect ('exceedingly likely') *B. Coli* in 100 Cc. main tap water in London.

Metropolitan Water Board Reports.

Dealing with *B. Coli*, taking one figure results, this organism occurs in raw Thames water to the extent of 19 organisms per Cc., Lea water 5 organisms per Cc., New River 2 organisms. For *filtered* waters a one figure result per Cc. of water—expressed as typical *B. Coli* per 1,000 Cc., gives Kent 1 to 2, West Middlesex 14, New River 2 to 3.—Sir A. C. Houston, B.M.J. ii./12,1671.

Raw Thames water in 1912-1913 contained 6,550 microbes per Cc., Lea water 11,772, New River 2,777. On filtering the figures were respectively 14.5, 30.5, and 12.6.—Sir A. C. Houston, B.M.J. ii./13,678.

The 1914 Report indicates that with the raw waters practically all contained *B. Coli* in 100 Cc.

About 70% and over (usually about 80%) of the filtered waters examined contained no typical *B. Coli* in 100 Cc. The following analysis is provided:—

RAW WATER.							<i>B. Coli</i> per Cc.	
River Thames	15
River Lea	5
New River	0.5
FILTERED.							<i>B. Coli</i> per 1,000 Cc.	
Kent and Chelsea	1 to 2
New River, E. London (Lea), Grand Junction, W. Middx., S. and Vauxhall	2 to 3
Kempton Park, East London (Thames), Lambeth	3 to 4
Lea, New River and Thames derived water, All London waters	2 to 3

FROM THE 10TH RESEARCH REPORT: In purified water, there is no possibility of cumulative microbial effect. It is stated further that more than one

Typhoid bacillus is needed to infect a susceptible person with typhoid and in no conceivable circumstances can the typhoid bacillus multiply in water.—Sir A. C. Houston, B.M.J. i./15,477.

Algæ in Water. POTASSIUM PERMANGANATE.—2·5 to 5 pounds per million gallons is efficacious in removing the nauseous taint due to *Algæ* in reservoirs—better than Hypochlorite.—Sir A. C. Houston, B.M.J. ii./16,817.

THE SIXTEENTH ANNUAL REPORT STATES: Although storage purifies the *Thames* water greatly, chlorination gives even better results. The *New River* water deteriorates during the flood months and it is then, unlike the case of the *Thames*, that chlorination is practised. *Chelsea Water*. An emergency measure was successful. The water was chlorinated after filtration and sometimes Permanganate was added.

Deptford Well. Minute doses of chlorine (0·25 per million) gave rise to taste trouble which could not be surmounted by concurrent use of Permanganate without giving a pink tinge. Chlorine 1 per million was then used with dechlorination by sulphurous acid with success.

A *protococcus-like* growth developed in the *New River* works during May 1921, which gave trouble.

Suspended Solids. Since Nov. 1920 gravimetric determinations of these in *Thames* Water have been made once a week. During periods of heavy rainfall temporary closing of intakes is indicated.—Sir A. Houston, L. ii./22,533.

THE SEVENTEENTH ANNUAL REPORT STATES: 80% of London's water supply comes from two rivers which are undeniably polluted. Less than 20% comes from the deep wells in Kent and in the Lea Valley. Another well (at Waltham Abbey) although bacteriologically very pure, contains Iron and Sulphuretted Hydrogen which have to be eliminated. *Chlorination* at *Staines* has been conducted without complaint. The *New River* supply—an artificial channel 30 miles in length, is practically free from pollution but contains *Algæ* (see above)—difficult to cope with.—Sir A. Houston, L. ii./23,341.

THE EIGHTEENTH ANNUAL REPORT STATES: It is very hard to associate typhoid fever causatively with the water supply in this country. The sea gull has made an attack on London water and has had to be frightened away, but so far as is known they do not suffer from water-borne diseases of man.—Sir A. Houston, L. ii./24,558.

THE NINETEENTH ANNUAL REPORT STATES:—In the *New River* heavy winter rains deteriorated the water, but chlorination remedied this. Objectionable taste in chlorinated water avoided by careful dosage and use of Permanganate (0·5 to 1 per million). The *New River* water has been chlorinated for 6 consecutive years without causing taste troubles. (?) Atmospheric pollution adversely affects water so treated, through absorption by the water of apparently phenoloid gases, causing an 'Iodoform' taste, but this does not occur when the water contains a trace of Ammonia; chlorinated water should not be mixed with water which has been so polluted. The *New* reservoir at *Littleton* doubles the storage capacity for *Thames* water. Sir A. Houston believes in the expediency of primary rapid filters, working at the rate of 100—200 gallons per sq. ft. per hour, as a preliminary to slow sand filtration, which, with the addition of chlorination, may thus be accelerated by two or three times or more. The *Thames* might be made a salmon river again.—B.M.J. ii./25,526.

THE TWENTIETH ANNUAL REPORT STATES:—In the *Palmer's Green* area in Dec., 1925, there was a slight breakdown in 'Taste' prevention, owing to the weather condition (cold fog, with decrease in organic matter). Heavy capital expenditure for larger storage accommodation and increased filter beds is avoided by chlorination, and filtration is carried on more rapidly. Preliminary rapid filters remove so much of the materials which choke slow sand filters that the latter can work five times as fast and enjoy a longer life. It is hoped that this double filtration process will prove more economical, but in some cases the economy may be neutralised by increasing pumping costs, and further experiments are being conducted in the inhibition of development of algal and other growths by the addition of minute doses of Copper Sulphate. Organisms which give water a fishy taste are *Eudorina*, *Pandorina*, *Uroglena*,

etc.; a taste like ripe cucumbers is caused by *Synura*; a grassy taste by *Alphanizomenon*, etc.; and an aromatic taste by *Asterionella*, *Tabellaria*, etc. A copious growth of the last-mentioned, due to raking operations (now discontinued) occurred in 1913, when the West Middlesex water was variously described as tasting like geraniums, rotten fish, and castor oil.

A new problem in water biology is the discovery of the presence of *leptospira*, which are almost universally present, equally in filtered waters and in pure deep wells as in raw sources of supply. All cultures have proved non-pathogenic, and the leptospira are easily killed by minimal doses of Chlorine. Sir A. Houston does not regard their presence as of any great significance, but the possibility of a change from a saprophyte to a pathogen opens disturbing possibilities. Rats may possibly be the cause, by poisoning water and slime.—B.M.J. ii./26,533. See also p. 610.

THE TWENTY-FIRST ANNUAL REPORT STATES:—Kent supplies a daily average of 27 million gallons (from 24 wells), which forms one-tenth of London's water supply. The water is clear, exceptionally pure, and is cool in hot weather. During 1926 the average bacterial counts were 9 per Cc. on gelatin and 0.05 on agar, with *B. Coli* absent from 100 Cc. in 94% of samples. The average figure for Ammoniacal Nitrogen was 0.0002 per 100,000, Albuminoid Nitrogen 0.0023, and for oxidised 0.6. The water from Deptford Garden Well was found to harbour a pathogenic leptospira, which cleared up after chlorination. Since 1916, two million people have been supplied with 76 million gallons of chlorinated water daily and no complaint of a taste has been made. During 1926, the Staines and Hampton water showed *B. Coli* absent from chlorinated water in 53 samples. 25,000 million gallons were chlorinated in 1926 at an average dose of 0.35 parts of Chlorine per million and a cost for chemicals of 1/- per million gallons, giving a nett saving of coal (for the purpose of pumping reservoirs) of £14,872. Rapid filtration experiments (at Barn Elms) continue to show satisfactory results.—B.M.J. i./27,1122.

THE TWENTY-SECOND ANNUAL REPORT STATES:—It is easier and more economic to purify a river after pollution than to prevent it from becoming polluted. The chlorination of Thames water continues at the rate of 10 million gallons daily. In 1927, Staines and Hampton water showed *B. Coli* absent in 66.8% of samples, and for filtered waters the figures were Kemptown Park 83.4%, Sunbury 77.8%, Grand Junction 75%, and West Middlesex 72%. The Stoke Newington Reservoirs (New River chlorinated water) only showed *B. Coli* absent in 21.9% of samples, but this is no new feature and is probably due to pollution flowing unseen into the water-way between Wood Green and the outlet. The storage reservoirs supplying London constitute a chain of 49 lakes, covering 2,700 acres and holding 20,000 million gallons of water. The Molesey was 1,000 times better than the raw water of the river, the former containing *B. Coli* in 100 Cc. in 39.1% samples, and the latter *B. Coli* in 0.1 Cc. in 50% samples. In other words, **it would be less risky to drink 50 pints of stored water than one ounce of the native Thames.** Experimental working at Barn Elms show that bacteriological quality of the final product is as good as with the ordinary once-through slow sand filtration, has more freedom than the latter from algal troubles and those caused by excess of suspended matters, and has a much greater output per acre of filtration area. At the Walton Works, opened July, 1926, this method of **double filtration**, preceded by storage and followed by chlorination, is put into practical operation; in 1927, final samples showed *B. Coli* absent in 96.4% as compared with 0.4% in raw river water. In 1927 frequent cultures of London waters were made for leptospira. These were numerous in the New River water, but disappeared after chlorination. In seven instances the organisms were pathogenic.—B.M.J. ii./28,500.

At a meeting of the Public Works, Roads and Transport Congress, Mr. I. Gibbon, of the Ministry of Health, recommended local authorities to have a policy of water supply outlined for 50 years ahead, and where neighbouring authorities have a common interest the appointment of regional committees.

Sir A. Houston said that already over **1/7 of the population of England are drinking** with impunity highly purified water from sources of questionable origin. If the absence of *B. Coli* from a water is to be taken as implying the absence of microbes

water-borne disease, this organism can be practically eliminated by storage and filtration, and with the addition of Chlorination can be completely eliminated. There have been cases abroad where the addition of Chlorine to impure water, previously responsible annually for an enormous amount of disease and death, has seemingly resulted in the almost complete elimination of water-borne diseases.—L. i./26,29.

The Ministry of Health has issued a booklet dealing in detail with the setting up of Regional Committees (H.M.S.O., Nov., 1928).

Anti-Bacterial Action of the water of certain French rivers.—These have inhibitive or actual destructive effect on growth of intestinal bacteria, *e.g.*, antagonistic action to *B. Coli* of the Saône, to *B. Typhosus* of the Rhône, *B. Paratyphosus A* of the Izère, and *B. dysenteriae Shiga* of the sea at Havre. May serve to explain why certain regions and persons are immune to water-borne diseases.—B.M.J.E. i./26,40.

EXCESS LIME METHOD of treating water is effective for sterilising and purifying, and when necessary **Softening** water.

Liming the Dee was a means of overcoming sewage pollution.

***Permutit** (T.M. 317579, 342540 Class I.) system of **Water Softening**. An artificial zeolite a compound of silica, alumina and soda. In contact with hard water it abstracts the Calcium and Magnesium constituting the hardness in exchange for a soda complement. The lime and magnesia are left behind in the cylinder and the corresponding sodium salts pass into solution.—L. i./15,214. For further details on water softening see Vol. I., p. 731.

Sewage (Crude).—Total organisms in London sewage found to be 6 to 12 millions per Cc. *B. Coli* never fewer than 100,000 per Cc.—Klein and Houston.

CHEMICAL AND BACTERIOLOGICAL EXAMINATIONS OF DRINKING WATERS COMPARED.

A water may pass certain standards chemically and yet be unsatisfactory from the bacteriological aspect. The converse may also be true in some cases. We made some combined investigations on these lines some years ago and in the table *postea*, are the more important data obtained. The Waters comprise a selection as supplied from the main to consumers in some of the leading cities and health resorts in Great Britain, including, *e.g.*, London, Glasgow, Bath, Blackpool, Buxton, etc. We concluded:—

(1). The bacteriological investigation is quite as useful as the chemical—and should always accompany it. (2). The absence of *B. Coli* from 100 Cc. of a water is an ideal seldom attained. (3). The albuminoid ammonia content is no indication of the number of bacteria, but in conjunction with Chlorine, Nitrite and Nitrate, data may suggest sewage contamination. (4). Examination of waters at the source and after traversing some miles of water supply pipes may show marked differences.

Speaking generally, these town supplies were of good quality.

CHEMICAL AND BACTERIOLOGICAL EXAMINATIONS OF DRINKING WATERS.

Source.	Chemical.				Solids parts per 100,000, and effect on ignition.	Bacteriological.										Conclusions	
	Ammonia. Parts per million		Chlorine parts per 100,000.	Bacteria per Cc.		Vol. producing Acid and Gas in MacConkey with		Indol Reaction.	Fluorescence on Reibel-agar plates.	Acid and Clot in Litmus Milk.		Motility					
						Free.	Alb.			Glu- cose†	Lac- tose†		Kosindol Reaction.	Indol Reaction.	Agar at 37° C.		Gelatin at 20° C.
Water																	
No. 1	Nil.	0.06	1	6	Much charred	100	160	Cc. 10	Cc. 10	+	+	+	+	+	+	+	Chem., Good. Bact., Not satisfactory.
No. 2	0.02	0.034	2	36	slight charring	972	8	100	100 50 acid only.	—	—	—	+	+	+	+	Chem., Excellent. Bact., Satisfactory.
No. 3	Nil	0.06	1.5	12	slight charring	1,209	57	10	50	—	+	+	+	+	+	+	Chem., Good. Bact., Satisfactory.
No. 4	0.03	0.12	1	15	much charring	45	80	None with 100 Cc.	None with 100 Cc.	—	—	—	—	—	—	—	Chem., Safe. Bact., Excellent.
No. 5	0.026	0.056	5	45	v. sh. charring	172	199	10	10	+	+	+	+	+	+	+	Chem., Good. Bact., Not satisfactory.

No. 6	Nil.	0.026	3	30 not charred	1,109	37	50	50	—	—	+	+	—	—	Chem., Excellent. Bact., Satisfactory
No. 7	0.026	0.03	1	3 charred	at least 1,000 some liquefng.	820	10	10	—	—	—	—	—	—	Chem., Excellent. Bact., Might be better.
No. 8	0.08	0.12	1.5	18 charred	at least 1,000 some liquefng.	1,600	50	50	—	—	—	—	—	—	Chem., Safe organi- cally. Might be better.
No. 9	0.01	0.036	6.5	45 v. sli. charring	1,040	242	50	50	—	—	—	—	—	—	Chem., Excellent. Bact., Satisfactory
No. 10 Village Well A	0.08	0.168	10.5	70 charred	10	60	1	10	+	+?	+	+	+	+	Chem., Unsatis- factory.
Ditto B	0.026	0.12	10.5	68 charred	B. Sub- tilis pre- vented count	75	100	100	+	—	+	+	+	+	Bact., Bad. Chem., Unsatis- factory.
No. 11	Nil.	0.11	1.5	6 Much charred	3,000	50	10	10	+	+	+	+	+	+	Chem., Safe organi- cally. Unsatis- factory.
No. 12* London A	1.	2.	3.	4.	5.	6.	7.	8.	9.	10	11.	12.	13.	14.	15.
	Nil.	0.04	1	32	less than 10	20	100	100	+	—	—	+	+	+	Chem., Excellent.
London B	Nil.	0.03	1	32	Nil.	21	100	50	+	+	+	+	+	+	Bact., Satisfactory.

*West London Main 2.29 Cl. per 100,000 and Solids 37 per 100,000.--W.H.M., January, 16/29.

Source.	Chemical.				Bacteriological										Our Conclusions.
	Ammonia. Parts per million.		Chlorine parts per 100,000.	Solids Parts per 100,000, and effect on ignition.	Bacteria per Cc.		Vol. produc- ing Acid and Gas in Mac- Conkey with	Rosindol Reaction	Indol Reaction	Fluorescence on Reibel- agar plates.	Acid and Clot in Litmus Milk.		Motility.		
	Free.	Alb.			Gelatin C. at 20° C.	* Agar at 37° C.					Glu- cose†	Lac- tose‡		Acid	
No. 13	Nil.	0.08	2	21 slight charring	1,400	1,350	10	10	+	+	+	+	+	Chem., Good. Bact., Not satis- factory.	
No. 14 Margate	Nil.	0.04	2.5	30 not charred	800	30	10	10	—	—	—	—	—	Chem., Excellent. Bact., Satisfactory.	
No. 15 Norfolk (Private well be- fore re- pair) Ditto (after repair)	0.026	0.076	4	40	52	32,000	1/100	1/100	+	+	+	+	+	Chem., Org. safe. Bact., Bad.	
	0.1	0.07	4	36	70	157	10	50	—	—	—	+	—	Chem., Org. safe Bact., improved, now safe, subject supervision.	

* Pathogenic and intestinal organisms grow best at this temperature.

† Presumptive evidence of *B. Coli*, *B. Paratyphosus*, *B. Enteritidis*, but excluding *B. Typhosus* and Dysentery Organisms.

‡ Confirmatory for *B. Coli* as *B. Typhosus*, *B. Paratyphosus*, *B. Enteritidis* and Dysentery organisms do not give it.

Columns 7 to 13 include the "Flaginac" Reaction.

Columns 9, 10, and 14 show results of cultures in peptone water from least quantity of MacConkey's Culture showing acid and gas.

Swimming Bath Water.

Chlorination of Swimming-Bath Water.—The water is circulated by a pump, passing first through a gauze strainer. It is then treated with an Alumino-ferric coagulant, to separate colouring matter and impurities, passed through closed pressure sand-filters, and aerated. Finally, it is treated with Cl_2 , about 1 part per 2 millions, and returned to the bath heated. Analysis of water so treated after 19 weeks' use at the St. Helen's Public Baths showed 112 bacteria per Cc. on Gelatin in 3 days, *B. Coli* and *B. Enteritidis Sporogenes* entirely absent in 100 Cc.; nitrites and free Chlorine were absent, and the free Ammonia was 0.0046 and Albuminoid Ammonia 0.0058 per 100,000. It is claimed that the process enables the same water to be used for twelve months at a time. (Apparatus supplied by the Paterson Engineering Co., Ltd., London).—B.M.J. ii./25,349.

Electrolysing of a mixture of Sodium and Magnesium Chlorides in production of a stable disinfectant—used at Poplar. F. W. Alexander's preparation is a hypochlorite relatively free from chlorate and rendered stable by a slight excess of the base. Used for swimming baths. A difficult problem to clean the water effectually.—L. i./26,357.

For a further abstract see *Edn. XVIII.*, p. 455.

MINERAL WATERS.

The following information regarding mineral waters has been obtained by applying in most instances direct at the sources.

The arrangement of the paragraphs is as follows:—

The name of the water and locality is given, then follow in order the names of spring or springs, the nature of the water, the chief chemical constituents, the medicinal uses, the season, if any, at the health resort, and an indication as to whether the water is imported in the bottled condition. The accounts of some are, however, condensed. 'Sulphurous' is to convey Sulphuretted Hydrogen with (usually Sodium) Sulphates and Sulphides.

***Trade Marks.**—A search has been made in Classes III. and XLIV on the Register for the purpose of this chapter.

Aedipsos (GRECIAN).—Saline, thermal. **Aegina** (GRECIAN).—Alkaline Imported.—Ph. Notes.

***Aesculap** T. M. 22666, Class 44; 185183, Class 3 (HUNGARY).—Magnesium and Sodium Sulphates, Sodium Chloride and Calcium Sulphate. Occasional and habitual constipation, bowel and liver disorders. Imported.

Aix-les-Bains (SAVOY).—Sulphur and an organic matter called Baregine, which renders it easy of digestion, oily and suitable for massage. Rheumatism, gout and throat diseases. 1st April to end of October. Also imported. Employed as tubs, shower bath, massage and vapour baths.—L. Blanc, L. ii./15, 174.

The distinctive feature of the Aix thermal treatment is the douche-massage known throughout the world as the Aix douche; the patient has streams of water directed on him while seated in a chair.—B.M.J. ii./21,118. See also Preston King, B.M.J. ii./25,635.

From the balneological aspect, the treatment par excellence for rheumatoid arthritis is the combination of douching and massage introduced from Aix-les-Bains.—R. Waterhouse, B.M.J. ii./25,596.

Alet (AUDE, FRANCE).—Source des Bains and Source Nouvelle.—Alkaline carbonated. Debility, dyspepsia, anæmia. Imported.

Allevard (ISERE, FRANCE).—Sulphurous carbonated. Calc. and Magnesium Bicarbonates, Sodium Chloride, Calcium, Sodium and Magnesium Sulphates, free Sulphuretted Hydrogen, Carbonic Acid and Nitrogen.

Chest affections of all kinds, skin diseases, women's diseases, rheumatic complaints, June 1st to September 30th, and imported.

Alvaneu-Bad (near ENGADINE).—Sulphurous. Alpine Climate.

Andros (GRECIAN).—Chalybeate.—Imported.—Ph. Notes.

***Apollinaris** T.M. 153705 and 283030, Class 44. (NEUENABR, GERMANY).—Acidulated alkaline table water. Sodium Chloride, Calcium and Magnesium Bicarbonates, with large excess of carbonic acid. Catarrhal affections of the respiratory organs and mucous membrane, acute and chronic laryngitis, bronchitis, dyspepsia, gout and gravel. Imported. See also Table of Waters.

***Aquaperia**. T.M. 363617, class 44. (HARROGATE, GT. BRITAIN).—A natural tonic aperient water, standardised and of high organic purity. Dose, a wineglassful before breakfast. For constipation, liver disorders and bilious complaints. Relieves gout and rheumatism and helps to prevent indigestion.

Ax-les-Thermes (PYRENEES). Altitude 2,000 ft. Alkaline Sulphur from a number of springs. Radioactive, organic matter termed *baregine*. Gout and rheumatism, respiratory troubles and skin affections.—L. ii./22,826.

The ground is warm with hot springs and the snow melts in consequence. Some of the springs are milky with Colloidal Sulphur. In other springs the alkalinity, due to Sodium Carbonate and Silicate and some Lithia, is pronounced. Professor C. Moureu has recently shown that the gas evolved from the Source Viguerie at Aix contains Argon and Helium, as well as Nitrogen. The composition of the gas was found to be :—Nitrogen 98·45%, Argon (with traces of Krypton and Xenon) 1·453%, Helium (with traces of Neon) 0·097%. The presence of the inert gases points to a radioactive origin, to which may be due the beneficial results from the treatment with the thermal waters. The curative properties have been known for a long time.—J. G. F. Druce, C.D., Mar. 12/27,323.

Bagnères-de-Louchon and Bagnères de Bigorre (WESTERN PYRENEES).—Alkaline sulphurous. Sodium Sulphide and H_2S . Gout, chronic rheumatism, respiratory and cutaneous troubles. Mid May to Mid October.—L. ii./22,880.

Baignes-de-L'Orn (NORMANDY, FRANCE) Grande Source.—Small quantities of Sodium Chloride, Sodium Sulphate and Silica, also traces of Potassium, Iron and Calcium Salts. Used chiefly as baths and douches but is also drunk. Palebitis, varicocele, women's diseases and rheumatism. May 15th to October 1st, imported.

Barèges (HAUTES - PYRENEES, FRANCE).—Sulphurous, warm. Sodium Sulphydate and Sulphate, Sodium Chloride, Silica. Chronic rheumatism, skin and bone diseases. Imported.

Barium (LLANGAMMARCH WELLS, WALES).—Saline. A tumbler full three or four times daily. Sodium, Calcium, Magnesium and Barium Chlorides. Good organically. Only 0·0056 grs. per gallon of Albuminoid Ammonia. Contains no sulphates owing to presence of Barium. Heart affections, glandular swellings, skin affections, rheumatism. Bottled, both aerated and still.

Bath. The only thermal spring in England, and one of the oldest in Europe. King's Bath Spring.—Calcium Sulphate 102·88 grains, Sodium Sulphates 23·5, Magnesium Chloride 15·8 grains, per gallon, and other Salts in less proportion. Radium has been found in the waters and deposits, also Argon, Helium, Krypton and Xenon.

King's Well contains 0·1387 mgr. **Radium** per million litres. If the Niton (emanation) were represented by the weight of Radium capable of forming the Niton present in a million litres of water or gas, the figures for the water of the King's Well, Cross Bath and Hetling Bath are respectively 1·73, 1·19, and 1·7 and for the gas from the King's Well 33·65. The gas from the King's Well contains about four times as much Niton as is contained in the natural gas from Buxton, viz., 7·7 and 8·5 mgr. per million litres. Further data Vol. II., XVIIIth Edn., p. 457. (See also SULIS, i.e., Bath water aerated and bottled.)

Ben Rhydding. See Ilkley.

Besançon (JURA).—Saline springs with bromides and iodides. Children's diseases and gynaecological conditions, e.g., sterility.—L. i./24,1037.

***Bethesda** (T.M. 171394). (WISCONSIN, U.S.A.)—Alkaline, Calc. and Mag. Bicarbonates. Kidney diseases, Bright's disease, diabetes, torpid liver, dyspepsia, insomnia. Imported.

Bilin (BOHEMIA).—Alkaline acidulated table water, Sodium Carbonate, Sodium Chloride, Sodium Sulphate, Lithium Carbonate, Free Carbonic Acid. Catarrh of the stomach and of the respiratory organs, rheumatism and for Bright's disease. Pastilles are also prepared.

Birmenstorf (SWITZERLAND).—Saline aperient. Constipation, jaundice, hæmorrhoids, uric acid. Imported.

Bonnes (see EAUX BONNES).

[P1] **Bourboule, La** (PUY DE DOME, FRANCE), Choussy-Perriere Spring.—Arsenated, 1 litre = 0.028 Gm. Crystallised Sodium Arsenate (1.9 grs. per gallon), Sodium Chloride and Bicarbonate. *Dose*, a large tumblerful. Debility, anæmia, chest affections, arthritis and diabetes. Imported.

Bourbon-Lancy. Oxygen is, in the majority of cases, absent in the gas of mineral waters, or present only in traces, but the gas of this spring contains 0.53%.—Prof. C. Moureau, C.D., June, '23, 869.

Braceborough (LINCOLNSHIRE, ENGLAND).—Known since the reign of George III. The spring gives 200,000 gallons a day at 50° F. Calcium Bicarbonate 30, Calcium Sulphate 6.6, Magnesium Sulphate 2.26 grains per gallon. Free CO₂ 2.1 grains per gallon. Bottled.

Dose.—One to 2 tumblersful first thing in the morning and at night.

In psoriasis, erysipelas, eczema, and other skin affections; also in nervous conditions.

Successful in gout. Relieved excessive micturition. Digestion improved.—A. Eddowes, Jl. Clin. Research, April, '25.

Brides-les-Bains (SAVOY, FRANCE).—Alkaline saline. Contains Sulphates of Sodium, Magnesium and Calcium, and Chloride of Sodium. Obesity, uric acid, hepatic complaints, gastro-intestinal diseases, constipation. Imported. Description of resort and water. Closely analogous to the Sprudel Source at Carlsbad.—B.M.J. i./20,545. See also L. i./24,1037.

Brucourt (CALVADOS, FRANCE). "Star" Spring.—Chalybeate. Tonic in anæmia. Imported.

Buffalo Lithia (MECKLENBURG CO., VA., U.S.A.).—(No. 2 the chief spring). Alkaline Lithiated table water. Albuminuria, uric acid diathesis, and other affections needing alkaline treatment. June 15 to October 1, and imported.

[P1] **Bussang** (VOSGES, FRANCE).—Ferruginous tonic and digestive. Free Carbonic Acid, Sodium, Calcium, Magnesium Bicarbonates with Manganese, Iron and Arsenic. Anæmia, chlorosis, jaundice, gout, rheumatism, diseases of women. Season, 15th June to 15th September, and imported.

Buxton (DERBYSHIRE).—Slightly Saline. Sodium Chloride, Magnesium Carbonate, Calcium Carbonate, Free Nitrogen and Carbonic Acid. Stomach, bladder, liver, and kidney disorders, skin affections, gout, rheumatism, sciatica, All the year round and bottled. See also Table of Waters.

The gentlemen's Natural Baths contain 1.1 mgr. per million litres of *Niton*, i.e., about the same as the Cross Baths at Bath.—Sir Wm. Ramsay.—B.M.J. i./12,617; L. ii./12,746; P.J. i./12,373.

Valuable in alleviating chronic articular gout and rheumatism—irregular forms of gout are benefitted and acute attacks cut short. The mineral constituents only amount to 27 grains per gallon, chiefly Carbonates of Calcium and Magnesium, Sodium Chloride with traces of Iron and Manganese. The gases contained show a unique richness in Nitrogen. So far as is known radio-activity exerts a healthy active influence over metabolism.

Buxton Mineral Water. As a result of experiments the following conclusions have been drawn: (1) It has a diuretic effect superior to distilled water, (2) It increased the elimination of Sodium Chloride, (3) It increased hydric concentration and favourably influenced metabolism.—L. ii./23,1301.

Buxton Water has a stimulant effect on Nitrogen metabolism and produces conditions favourable for more complete oxidation.—B.M.J. i./24,17.

MINERAL WATERS AS DIURETICS. The aim of their employment in diuresis is to promote the excretion of harmful solids, rather than the mere excretion of water, and for this purpose mineral waters of low concentration have been found superior to distilled water. The total amount of salts in a dose of mineral

water which would produce diuresis is very much less than that required in an artificial solution. Three types of mineral waters possess diuretic properties—sulphur water, including the sulphuretted salines, the calcareous and the radio-active thermal waters of low mineralisation.—C. W. Buckley, L.i., 23,1300.

*** Cachat** T.M. 293559 and 293558, Class 44 (*see* EVIAN, Source Cachat).

Capvern (HAUTES PYRENEES, FRANCE).—2 springs; Houn-Caoude (drinking) and Bouridé (baths). Alkaline. Catarrh of bladder, gravel, gall stones, women's diseases. Season, May to October. Imported.

Carabana (SPAIN).—Purgative. Sodium Sulphate. Intestinal and hepatic affections and dyspepsia. Imported.

Cauterets (PYRENEES).—Sulphurous. Sulphuretted Hydrogen, Iodine. Skin and lung diseases, glandular swellings. Summer and imported.

The gas given off at the spring by this mineral water consists of 98.55% Nitrogen.—Prof. C. Moureau, C.D., June '23, 869.

Cerigo (GRECIAN).—Chalybeate. Imported.—Ph. Notes.

Challes (SAVOY).—Sulphurous. Chronic catarrh, skin affections and intestinal diseases. May to October. Imported.

Chateldon (PUY DE DOME, FRANCE).—Alkaline Acidulated. Stomach and urinary disorders, anæmia, and as a table water. Imported.

Chatel Guyon (AUVERGNE, FRANCE). Source Gubler.—Alkaline. Dyspepsia, jaundice, anæmia, constipation, uric acid, May to October. Imported.

Cheltenham—Pittville Waters: No. 1 Chelt. Alkaline, Sodium Chloride, Sulphate and Bicarbonate; No. 2 less Sodium Chloride, more Sulphate; No. 3 more Sodium Sulphate but less than No. 2; No. 4 Cheltenham 'Magnesia' (Magnes, Sulphate 117 grains per gallon) and Sodium Sulphate, No. 5 is No. 4 concentrated. No. 6 is Cheltenham Sodium Sulphate Saline, Sodium Sulphate in predominance. *See also* Table of Waters and P.J. ii./15,571.

Claudia (SORGENTE DI ANGUILLARA, SABAZIA, near ROME).—Alkaline. Carbonic Acid with small quantities of Alkaline Bicarbonates. Gastric dyspepsia. Imported.

Condal (RUBINAT, LERIDA, SPAIN).—Aperient, Sodium, Magnesium, Calcium and Potassium Sulphates, Sodium Chloride. As a purgative for habitual constipation, plethora, etc. Imported. *See also* Table of Waters.

Condillac (FRANCE).—Alkaline acidulated table water. Imported.

Contrexeville (VOSGES, FRANCE). Pavillon Spring.—Alkaline, Antirheumatic. Gouty affections, dyspepsia, eczema, catarrh of the bladder and liver. 20th of May to 20th of September, and imported. Contrexéville Source Mignon is also supplied. *See also* Table of Waters.

Why does Contrexeville water, containing much Calcium cure or alleviate gout? Probably it is not so much the Calcium content of the water as its influence on metabolism.—F. E. Tylecote, M.P., Mar. 27, '29, 261.

Coulsworthy (North Devon).—Alkaline. Detergent, osmotic and diuretic.

Dax (called locally La Néhe). Thermal—has temperature 61° C. Owing to evolution of Nitrogen appears to be boiling. Contains Sulphates and Chlorides of Calcium and Sodium. The mud contains a large proportion of living algæ—the *Oscillaria calida*. Is distinctly radio-active. In rheumatism.

Desaignes (Eau de César) (ARDECHE, FRANCE).—Alkaline, Acidulated Table water. Imported.

Dolecoed. *See* Llanwrtyd.

D'Orezza (CORSICA). Chalybeate table water. Anæmia, dyspepsia; useful after prolonged illness, or for weakness. 1st July to 1st September. Imported.

Droitwich. *See* *Wychia.

Eaux Bonnes (BASSES PYRENEES, FRANCE).—Mild Sulphurous. Helium is given off by the water—due in all probability to radium-containing mineral at the source. Similar to Baresges and Cauterets. Bronchial catarrh, phthisis, neurasthenia, asthma. June 1st to October 1st, and imported.

Has reputation of curing sterility in women. *cf.* Franzensbad.

Enghein-les-Bains (near (PARIS).—Sulphurous. Lung and skin affections, uterine disorders, nervous diseases, nose and ear affections. Season, May 1st to October 15th. Imported.

Epidaurus (GRECIAN).—Imported.—Ph. Notes.

* **Esvach** (T.M. 224276).—Aperient. Magnes. Sod. and Pot. Sulphates and Bicarbonates, free Carbonic Acid. Habitual constipation, indigestion, biliousness, gout. Bottled.

Evian-les-Bains (HAUTE SAVOY) Sources "Cachat" and La Croix.—Alkaline table water. Calcium and Magnesium Bicarbonates, free Carbonic Acid. Liver and intestinal disorders. For washing out bladder in uric acid troubles; calculi, cystitis. May to October.

Fango Mud Springs (ITALY).—Installation at Matlock. For the treatment of rheumatism.

Farris (Norske Mineralkilder, Larvik, Norway).—Mineral Table Water, radioactive, gout and rheumatic complaints.

Fayet St. Gervais (Savoy).—Saline and Sulphur springs, for arthritic troubles, skin-diseases, rhino-pharyngitis and neurasthenic conditions.—L. i./24,1037.

Fiuggi (ITALY).—Saline. Sodium Chloride, Potassium Nitrate, Calcium Carbonate, Carbonic Acid, Ozone, and Oxygen (possibly due to action of radium emanations contained), Nitrogen. Gastric complaints. Imported. Full report on.—L. ii./07,915.

Flitwick (near AMPTHILL, BEDFORDSHIRE).—Ferruginous. Ferric Persulphate and Sodium Sulphate. Anæmia, chlorosis, dyspepsia, general debility and neuralgia. Bottled.

Folkestone contains about $2\frac{1}{2}$ to 3 grains of chalk per pint—if boiled about $\frac{1}{2}$ grain—which cannot be considered deleterious or have any bad effect. Folkestone water is exceedingly pure containing a trace only of Free Ammonia and 0.0008 grain per gallon of Albuminoid Ammonia. Total Hardness 18.7. Permanent Hardness 2.9 grains per gallon.

* **Fontalis**.—T.M. 242666 and 251903, Class 44.—A pure table water. Alkaline. Chlorides and Carbonates, free from Lime and Magnesium Salts. Bottled at Harrogate.

Forges (NORMANDY).—Chalybeate. Ferrous Bicarbonate. Chlorosis, dyspepsia. Season, June 1st to October 1st. Imported.

Gilgit (KASHMIR, INDIA).—Goitre does not occur among the coolies who drink the pure water of the Gilgit river. Total solids 7 grs. per gall. Total Hardness 4, Calcium about 6, free ammonia and organic matter nil.—L. ii./06, 1570.

Grassion (FRANCE).—Bituminous. Throat and chest affections, gastric and vesical catarrh. Imported.

Gytje.—A kind of mud from the Norway fjords used in the "Gytje" treatment in balneology for gout and rheumatism.—Ph. Notes.

Harrogate (YORKSHIRE).—Sulphurous. Skin and rheumatic affections, e.g., eczema, psoriasis, lupus erythematosus, furunculosis, urticaria; also in anæmia, dyspepsia. Aperient and diuretic. Summer and winter, and bottled. The Sulphur and Alkaline Carbonates compose half the solid ingredients. The Beckwith Spring contains large proportion of Magnesia. Helium has been traced in the gases rising, hence presence of Radium is assumed. Sulphuretted Hydrogen content has been stated as 10.46 cubic inches per gallon. Some pharmacological effects of the Strong Sulphur Water.—D. Brown, B.M.J. i./11,1304.

Description of the Spa.—B.M.J. ii./19,78.

Barium in Harrogate waters. Stimulant action on muscular tissue, Barium content: 'Old Sulphur' Spring 6.91, 'Chloride of Iron' Spring 3.51, 'Magnesia' Spring 3.97, per 100,000.—A. Woodmansey, L. i./23,22.

"**Harrogate Salts**."—Potassium Tartrate 360 grains, Magnesium Sulphate 1 pound, Sulphurated Potash 1 ounce —P.J. i./07,548.

Hathorn (see SARATOGA).

"**Hygyn**."—A natural alkaline spring water from Rickmansworth, Middlesex, England, containing a small amount of added Sodium Hyposulphite. Suggested for cases of "blood pressure" and as an internal antiseptic.

Hypate (GRECIAN).—Sulphurous. Imported.—Ph. Notes.

Igmandi (KOMAROM, HUNGARY) Water. Radio-active. Saline aperient. Magnesium Sulphate 29·3, Sodium Sulphate 9·5, Calcium Sulphate 0·7, Sodium Chloride 0·8%. Total solids 40·8 per 1,000 Gm. Radio-activity inherent in the Calcium Sulphate.—L. ii./05,777 Corpulency, constipation, hæmorrhoids, rheumatism.

Ilkley and Ben Rhydding (ILKLEY in WHARFDALE). Chalybeate and Antacid. (i.) Chalybeate Spring. Ferrous Carbonate, Calcium Sulphate, and Alkaline Chloride. (ii.) “Hygeia” Spring. Calcium, Sodium and Magnesium Carbonates, Sodium Sulphate. (iii.) “Ilkley Wells” Gout and rheumatism.

Ilkley Wells (Old White Wells).—The composition from the content of Acids and Bases would appear to be Ferric Oxide 0·0159, Calcium Carbonate 0·3078, Calcium Nitrate 0·014, Calcium Silicate 2·0535, Calcium Sulphate 0·5199, Magnesium Carbonate 1·4235, Magnesium Sulphate 1·09, Potassium Carbonate 0·1548, Sodium Carbonate 0·8726, Sodium Chloride 1·155, *Lithium Chloride* 0·0831 grains per gallon.—B. A. Burrell, Yorkshire Geolog. Soc., 1914. *See also Health Resorts.*

Insalus (Spain).—Alkaline, Carbonated. Affections of the stomach, urinary passage, kidneys and bladder.

Kyllini (GRECIAN).—Sulphurous. Imported.—Ph. Notes.

Kythnos (GRECIAN).—Saline, Thermal. Imported.—Ph. Notes.

Labassère (HAUTES PYRENEES).—*See Bagnères de Bigorre.*

La Preste (EASTERN PYRENEES about 50 miles from Perpignan).—In affections of the urinary tract—cystitis, vesical catarrh, prostatitis, etc. Contains only 11·2 grains per gallon total solids. Silica one of the leading constituents.

Latraki (GRECIAN).—Alkaline.—Ph. Notes.

Leamington.—Saline. Calcium, Magnesium, Strontium and Barium Sulphates, Sodium, Calcium, Magnesium and Potassium Chlorides, Magnesium Bromide and Iodide, Calcium and Iron Carbonates with traces of Manganese and Titanium.—S. H. Smith, 1914. Dyspepsia, gout, women's diseases, sciatica, glandular swellings and skin diseases. Bottled. *See also Table.*

[F]Levico (AUSTRIAN TYROL).—Two springs (strong and mild); Arsenical chalybeate. STRONG: Arsenious Acid; 0·99 part per 10,000—1·12th of a grain per pint; the MILD is 1·10th of this. Further constituents: Ferrous Sulphate, and Ferric Persulphate. Anæmia, skin eruptions, neuralgia and amenorrhœa.

Llandrindod (WALES).—“Strong Sulphur,” “Roman Spring,” “Magnesium Spring.” The first is radio-active. In skin affections, dyspepsia, glandular enlargements, gout, rheumatism. Season all the year round.

The Sulphuretted Hydrogen waters are of several strengths. One contains a small amount of thallium chloride and a considerable quantity of lithia—latter higher than Royat.—B.M.J. i./09, 1245.

Llangammarch.—*See Barium.*

Llanwrtyd, Dolecoed Spa (WALES).—Sulphuretted Hydrogen, the strongest in Great Britain.

Louche (Leuk or Loeche les Bains) (VALAIS, SWITZERLAND).—Warm, almost exclusively for baths. Calcium Sulphate, Magnesium Sulphate, similar to that of Bath in England. Rheumatism, gout, women's diseases, skin affections. 1st May to 15th October.

Magnaris.—A table water prepared at Llandrindod.

Malvern (WORCESTERSHIRE).—Practically free from saline matter. Total $\frac{1}{4}$ grain per gall. only, and contains no organic matter. Bladder and kidney diseases and skin affections. Bottled.

***Malvern Selzer (T.M. 4744 and 5).**—Slightly saline table water.

***Malvernia.** T.M. 52502 and 86755, Class 44 (St. Anne's Spring, Malvern). A sparkling water, very saline, containing Calcium Carbonate 3, Magnesium Carbonate 2, Sodium Chloride 10, and Sodium Sulphate $\frac{1}{4}$ grain to the pint, together with a trace of Silica. Bottled.—L. i./26,350.

Marcols (ARDECHE, FRANCE), Source du Lion.—Alkaline table water. Stomach, liver and kidney diseases, rheumatism. Imported.

Martigny (VOSGES). Lithiated. Gravel, diabetes, liver and kidney complaints.

Methana (GRECIAN).—Sulphurous.—Ph. Notes. So powerful as to render the place objectionable; the sea into which the water falls is milky, owing to the decomposition of the sulphuretted hydrogen. The bacterium *Beggiatoa nivea* is found in the sediment, and in the protoplasm of this organism particles of sulphur are distinctly visible under the microscope. Imported.

Miers (LOT, FRANCE).—Saline, laxative. Sodium Sulphate, Calcium Sulphate, Magnesium Chloride. Dyspepsia, calculi, migraine, obesity, albuminuria. Imported.

Missisquoi (VERMONT, U.S.A.).—Sulphurous. Scrofula and other skin affections, diseases of respiratory organs. Imported.

[P] Mont Dore (PUY DE DOME, FRANCE).—Alkaline, Saline. Bicarbonates, Ferrous Carbonate, Arsenic, and Silica. Intestinal disorders, rheumatism, asthma, bronchitis and laryngitis. June 1st to September 20th. Imported.

Montmirail (FRANCE).—Sodio-sulphated. Mild aperient.

Montreux (SWITZERLAND).—Alkaline table water. Slightly mineralised: Stomach, liver, kidney and bladder affections. Imported.

Nocera Umbria (Angelica Spring, 185 kilometres from ROME).—Alkaline. Bicarbonates. Digestive, anturic, tonic, refreshing. Imported.

Orezza.—See **D'Orezza**.

*** Osmos (T.M. 386477).**—Mag. Sulph. (anhydrous) 1.73%, Sodium Sulphate (anhydrous) 1.79%, Sodium Chloride 0.16, Sodium Bicarbonate 0.18, Potassium and Calcium Salts—traces. Equivalent to Hunyadi Water.—B.M.J. ii./19,346. Used for constipation, dyspepsia, obesity, hæmorrhoids, liver and kidney disorders.

Ostend (BELGIUM).—In the Parc Léopold is an artesian well yielding a radioactive water, practically free from lime and rich in boron (0.1494 Gm. Sodium Biborate per litre) hence unique in this respect; containing also Sulphates, small amounts of Iodine, Bromine and Arsenic together with dissolved gases: Nitrogen 17.95 Cc. per litre, Argon 0.388, Helium and Neon 0.0194 and Hydrogen Sulphide 3.257 Cc. per litre. Internally or as baths in arthritis, obesity, diabetes, gastro-intestinal and genito-urinary affections, anæmia, skin and mucous membrane affections, pharyngitis and laryngitis. Contraindicated in tuberculosis and rachitis.—P.J. i./25,609.

*** Perrier (T.M. 287950 and 1).** (VERGESE, nr. NISMES, FRANCE).—Slightly mineralised, organically pure. Small proportion of Alkaline Carbonates. Digestive.—M.P., June 22/04.

Pistany (previously called Postyen).—A few miles from Vienna. Thermal mud baths, in rheumatic affections. For cases of sciatica and chronic periostitis also internal catarrhs.—B.M.J. i./20,545. Imported.

[P] Plombières (VOSGES, FRANCE).—Mild Saline. Sodium Sulphate, Arsenic, Oxygen, Nitrogen. Neurasthenia, gastralgia, dyspepsia, dilation of the stomach and chronic diarrhoea, rheumatism, skin affections. May to September. Imported. Mucous colitis is treated by washing out the colon with the alkaline sulphur water and further bath treatment.

The gas given off at the spring by this mineral water contains 1.64% Argon, with traces of Krypton and Xenon.—Prof. C. Moureau, C.D., June '23,869.

Poland (U.S.A.).—Potassium Sulphate, Sodium, Calcium and Magnesium Carbonate. In dyspepsia. Imported.

Postyen see **Pistany**.

Pougues (FRANCE).—St. Leger Spring.—Alkaline. Dyspepsia, anæmia, scrofula, gravel, catarrh of the bladder. May 15 to Sept. 30. Imported.

*** Presta.** T.M. 267852, Class 44. Raised by artesian boring (500 ft. deep) at Colindale, Hendon, N.W. London. It is therefore filtered through the natural chalk of the Chilterns on one side and the North Downs on the other; Bottled and used in making cordial waters—Lemonade, Ginger Beer and Ale. Lemon Squash, etc.

Pyrmont (WALDECK, WESTPHALIA). Three springs. HAUPTQUELLE contains most iron.—Chalybeate. Chronic catarrh, digestive and urinary diseases, women's diseases, scrofula, rheumatism and gout.

Quicherat (FRANCE).—Ferruginous. Magnesium and Sodium Chlorides, with some Iron and Manganese, Carbonic Acid. Anæmia, stomach diseases. Imported.

'Radium Water.'—From springs at Chao da Pena. Invigorating—advocated for rheumatism, sluggishness of gland action, faults of skin and hair, obesity, deterioration of nerves and arteries. Imported.

Ragaz-Pfäfers.—Canton St. Gall, Switzerland. Thermal Spring 99° Fahrenheit. Calcium, Magnesium, and Sodium Chlorides, Bicarbonates, and Sulphates. Very free from bacteria. Rheumatism, gout, sciatica, neuralgia. General season May to October, but a Spring Season begins middle of March. The waters belong to the simple Thermal group. Description.—B.M.J. ii./21,327.

Recoaro (VENETIA, LOMBARDY).—Sources: Lelia, Lorgnia and Giuliana.—Ferruginous Table Waters. Sulphates. Intestinal and liver complaints. Tonic, easily assimilated. Summer and imported. ROYAL BITTER SOURCE.—Is pure bacteriologically. Purgative for intestinal complaints.

Rennine (REIPERTSWEILER, ALSACE).—Nitrated. Potassium Nitrate 0.19 Gm. per litre. Alkaline Chlorides. Diuretic, laxative, in heart disease.

Renaion (FRANCE).—Alkaline, acidulated table water. Bicarbonates, free Carbonic Acid. Dyspepsia and gastric disorders. Imported.

[P] Roncegno (VALSUGANA, SOUTHERN TYROL).—Each litre contains 0.109 Gm. Sodium Arsenate, 0.115 Gm. Arsenic Anhydride, 0.03 Ferric Phosphate, 3.12 Gm. Ferric Sulphate, also Sulphates of Copper, Magnesium, Nickel and Cobalt.—From information provided by the local authorities.

Has the highest content of Arsenic in any spring, viz., 42.6 mgr As_2O_3 per litre.—P.J. i./12,689.

In addition to 0.007% As_2O_3 , O. Bennett found 0.004% Antimony Oxide.—P.J. ii./12,286.

[P] Royat (PUY-DE-DOME, FRANCE). Three Springs.—Saline, Arsenated (small quantity), Lithiated. Rheumatism, dyspepsia, nervous diseases, women's diseases, anæmia, skin affections and debility. Summer. Imported. Full description of this water.—B.M.J. i./07,758.

Rubinat (PYRENEES, SPAIN) "Llorach" Spring.—Aperient. Rich in Sodium Sulphate 9.62% and Magnesium Sulphate 0.32%, and contains Calcium Chloride. Stomachic disorders, constipation, liver and kidney affections. Imported. See also Table of Mineral Waters.

Rubinat (SERRE).—Similar to the last mentioned, but stronger than the above in the proportion of Sodium Sulphate to Magnesium Sulphate. Uses similar to the above. Imported.

[P] Saint Boès (BASSES-PYRENEES, FRANCE).—Bituminous, Iodised, and Arseniated. Arsenic, Iodine. Skin, lung, and venereal diseases. Imported.

Saint Galmier (LOIRE, FRANCE).—"Badoit" Table water. Dyspepsia, intestinal catarrh, constipation, nervous disorders, hyperæmia. Imported. "Noel"—Alkaline. Acidulated. Uses as latter. Imported.

Saint Gervais (HAUTE SAVOIE).—Saline. Sodium and Calcium Sulphates, Sodium Chloride. Skin affections, constipation, rheumatism and nerve diseases. 15th May to 30th September. Imported.

Saint Moritz (SWITZERLAND). "Paracelse" Spring.—Alkaline, Chalybeate, Tonic. Nervous and intestinal disorders, sick headache, hysteria, Graves' disease and for convalescence. All the year round. Imported.

Saint Sauveur—See Vernet les Bains.

Salies de Bearn (FRANCE).—Saline. Sodium Bromide and Iodide. Skin affections and as a general tonic.

Salins les Bains (JURA, FRANCE).—Tonic. Magnesium Chloride, Iodides and Bromides. Anæmia, tuberculosis, general debility, women's diseases, obesity, and scrofulous affections. Summer. Imported.

Salins Moutiers (SAVOY).—The French rival of Nauheim and Kissingen; Chloride of Sodium Carbonate of Iron, Arsenate of Sodium, Carbonic Acid and radio-active substances. Peculiarly adapted, together with Brides-les-Bains, for Anglo-Indians.—L. i./24,1037.

Sallyco.—Artificial. Is stated to contain Colchicine and Salicylic Acid.

***Salutaris** T.M. 151567, 308459 and 312724, Class 44.—Still and aerated table water, distilled water. For washing out the system in kidney and liver disorders, also gout and dyspepsia.

San Pellegrino (near MILAN).—Diuretic Calcium and Magnesium Sulphates, some Carbonate with trace of Chloride, also Lithium. Mineral Salts amount to 1.264 Gm. per litre.

Santenay (FRANCE).—The gas given off at the spring by this Lithium Water contains 10.16% Helium with traces of Neon.—Prof. C. Moureau, C.D., June '23, 869.

Saratoga (U.S.A.). "Congress" and "Hathorn" springs.—Alkaline, Saline. A mild aperient in dyspepsia, skin affections, diseases of the stomach, liver, kidney, and blood, constipation. Imported.

Siculia Water from Malnasi, Transylvania. A Roumanian water advertised for gout, rheumatism and lung and throat diseases.—C. D., May 27/22, 68.

Slanic Spa (ROUMANIA).—Rich in Carbonic Acid, Alkaline. Stimulates secretion by content of Sodium Chloride. **Antacid.**

Soulac-sur-Mer (MEDOC, GIRONDE, FRANCE).—Health resort. Sea air.

Spa (BELGIUM).—Ferruginous. Anæmia, uterine and nervous disorders, rheumatism, gout. Summer, and imported.

Strathpeffer.—See British Health Resorts.

***Sulis.** T.M. 46734 and 269024, Class 44 (Bath Water, aerated).—Aperient table water. Calcium and Sodium Sulphates, Magnesium and Sodium Chloride. Gives a radio-active emanation.

***Tansan.** T.M. 316950 and 319507, Class 44.—A Japanese water, radio-active. Radioactivity stated to be 31 Mache Units. A tonic table water. Imported.

Tarasp (LOWER ENGADINE, SWITZERLAND).—St. Lucius Spring.—Sulphated Alkaline. Rich in Sodium Sulphate, Bicarbonate and Chloride. Diuretic. Useful in chronic catarrh of the stomach, dyspepsia, gastralgia, habitual constipation, disorders of nutrition, obesity. 1st June to 15th Sept. Imported. Recent description.—B.M.J. ii./21, 328.

Thonon (LAKE LEMAN, FRANCE). Alkaline, Carbonated and Benzoated (Balsamic resins are contained). In liver complaints and urinary diseases. Imported bottled.

***Tonlaka.** T.M. 262400, Class 3; 449507, Class 44.—An alkaline tonic aperient water. Supplied in syphons and bottles.

Trefriw Wells near Llandudno, contain iron in ferrous state. One well showed iron in this form equivalent to 2.21 grains per ounce of crystalline ferrous sulphate, the other 1.42 grains. Dose, $\frac{1}{2}$ ounce twice daily.—B.M.J. i./19, 712.

Tsagesi (GRECIAN). Chalybeate.—Ph. Notes.

Uriage (FRENCH ALPS).—There are two springs, an iron spring containing Bicarbonate of Calcium and Sulphates of Calcium and Magnesia, and a Sulphur spring containing Hydrosulphuric Acid and Sodium Monosulphide. Useful for scrofulous children, congenital syphilis, glandular diseases, skin diseases and neurasthenic conditions.—L. i./24, 1037.

The waters considered to facilitate absorption of Mercury.—D. Freshwater, Pr., Mar., 1912.

Vals (ARDECHE, FRANCE). Springs: Madeleine, Précieuse, Désirée, Rigolette, St. Jean.—Alkaline, acidulated. (Contents vary with the spring.) Rheumatism, anæmia, skin affections. Imported.

Vange (ESSEX, ENGLAND).—Resembles many aperient Continental waters, e.g. those associated with Franz Josef, Hunyadi Janos and Seidlitz.

The true Vange Water (Farmer Cash's Well) is much more concentrated than Hockley Water. It contains Calcium Carbonate 46.5, Calcium Sulphate 88.7, Magnesium Sulphate 495, Potassium Sulphate 38.4, Sodium Sulphate 144.8, and Sodium Chloride 60.3 parts per 100,000. The Hockley Water contains Calcium Carbonate 46, Calcium Sulphate 57, Magnesium Sulphate 144 and Sodium Chloride 61 parts per 100,000. Analysis of other Essex Springs.—J. C. Thresh, P.J. ii./22, 557.

The supply of the true sulphated water is about 200 to 300 gallons per day.—J. C. Thresh, L. ii./22,1258.

Discussion of theory of action of mineral waters.—L. ii./22,724.

Vernet-les Bains (PYRENEES ORIENTALES).—Sulphate. Sodium Sulphate and Thiosulphate. Constipation, skin affections, anæmia. May to October, and imported.

Vernet-les-Bains Springs described.—L. ii./22,825.

***Vichy**. T.M. 312342-3, 46155 and 46158, Class 44. (ALLIER, FRANCE). Springs: Grande Grille, Hopital, Célestins, Parc.—Alkaline, acidulated. Gravel, chronic urinary affections, diabetes, female complaints, gout, rheumatism, facilitates digestion. May 15th to September 30th, and imported.

For renal elimination but does not appeal to English visitors.—L. ii./22,1276.

The gas given off at the spring by the mineral water at the source Chomelle contains 0.16% Nitrogen.—Prof. C. Moureau, C.D., June '23, 869.

The composition of Vichy Water, according to Sir James Barr, is, in grammes per litre, Bicarbonates of Soda 5.6, Potassium 0.35, Lithium 0.012, Calcium 0.36, Magnesium 0.07, Iron (-ous) 0.001, Sodium Chloride 0.57, Sodium Sulphate 0.28, Silicon Oxide 0.06, free Carbon Dioxide 0.97. The water is isotonic with the blood serum.—B.M.J. i./27,1063.

Villacabras (SPAIN).—Saline aperient. Sodium Sulphate. Obesity and constipation. Imported.

Analysis shows Sodium Sulphate 78.51, Sodium Chloride 1.05, Magnesium Sulphate 2.74, Calcium Sulphate 1.70 Gm. per litre. Replaces bitter waters of Germany, Austria and Hungary.—L. ii./15,184.

Vittel (VOSGES, FRANCE). Spring: Grande Source.—Alkaline: Sodium and Magnesium Bicarbonates, Sodium Calcium, and Magnesium Sulphates; Carbonic Acid. Uric acid, scrofula, chlorosis, biliary and urinary congestion. In addition are Source Salée, stronger in Magnesium Sulphate; Source Marie and Source des Demoiselles, Chalybeate. The first two are imported.

***White Rock**. T.M. 240106, Class 44. (U.S.A.).—Lithiated, gaseous. Table Water.

[P] Woodhall (LINCOLNSHIRE).—Saline, Bromo-iodised. Bromide, Iodine (free and combined), Sodium Chloride, Arsenic. Gout, sciatica, rheumatism, skin affections, goitre, women's diseases.

A large range of diseases from arthritis to eczema may be treated on orthodox principles.—L. i./29,1478.

***Wychia** (T.M. 274130) (DROITWICH).—Saline. Sodium Chloride 11.93 and Sulphate 7.89 per litre. Droitwich water is distinctly radio-active. Laxative in habitual constipation and plethora.

The Water is stated to be of specific value in gout, rheumatism and renal dropsy. Dose of the water is $\frac{1}{2}$ to 1 tumblerful, two or three times a day.

Droitwich Brine Baths have no equal for treatment of sciatica and allied affections. Even rheumatoid arthritis is certainly improved and in some cases actually cured. The cures of chronic sciatica are most striking.

Analysis of the brine has shown it to contain 20,000 grains per gallon of saline constituents in excess of that possessed by any other known water. The actual figures are: Chloride of Sodium, 21761.8; Chloride of Magnesium, 2.5; Sulphate of Lime, 91.1; Sulphate of Alumina, 14.4; Sulphate of Soda, 342.7; Iodide of Sodium, 0.208; total salts to an imperial gallon, 22212.8.

The brine acts possibly by absorption through the skin because the acidity of the urine is diminished, the output of uric acid being eventually lessened. Patients soon remark the change of colour in their urine, and the absence of pink deposit so well known in lithæmia. Urates are increased at first, and afterwards, as the urine becomes alkaline, they become diminished. The brine acts as a powerful uric-acid solvent. The radium emanation contained has something to do with this. Wonderful results in neurasthenia. Certain diseases are aggravated by the brine, e.g., malignant disease. The brine will cure almost every variety of uric-acid disease, both those belonging to the collæmic, and also to the arthritic group.—Jl., R.A.M.C., July, 1911.

Imported bottled mineral waters classified according to chemical composition.—A. E. Mix and J. W. Sale, Jl. A.M.A. ii./25,1964.

A Table of certain Mineral Waters showing their Approximate Contents in Grains per Pint.

SPRING.	CHARACTER.	CARBONATES (more or less in form of Bicar- bonates).	CHLORIDES.	SULPHATES.	OTHER CONSTITUENTS AND AUTHORITY.
Apenta	Saline Aperient.	Sodium, 4. Magnesium, 1½. Calcium, 1. Ferrous, ¾	Sodium, 15½.	Magnesium, 18½. Sodium, 164. Calcium, 23. Potassium, ¾ Lithium, ⅓.	Traces of Bromide, Alumina, etc.—R. C. Tichborne,
Apollinaris	Table Water.	Magnesium, 3¼. Calcium, 2¼. Sodium, ¾.	Sodium, 3½.	Sodium, 2.	CO ₂ (Free) 24½.—Apolli- naris Co.
Bath	Table Water.	Calcium, 1.	Magnesium, 2. Sodium, 2.	Calcium, 11½. Sodium, 3. Potassium, 1.	Traces of Iron, Ammonia, Nitrates. See also List <i>antea</i> .
Buxton (St. Anne, Ther- mal)	Slightly saline gas- eous table water.	Calcium, 1½. Magnesium, ¾.	Sodium, ½. Ammonium, ¼. Magnesium, ¼.	Sodium } Potassium } Calcium }	Traces of Iron, Manganese and Barium, Sulphates See also List <i>antea</i> .
Buxton (Chalybeate)	Chalybeate	Ferrous, ¾. Magnesium, ¼	Sodium, ¼.	Calcium, 1½. Magnesium, ½ Sodium, ¼.	Traces of Aluminium and Potassium Salts.
Cheltenham	Saline Aperient	Calcium, 4½.	Sodium, 3.	Magnesium, 14½. Ca., 8. Na., 7½.	Traces of Al., Fe., Mn., Brom- ides, Iodides, Phosphate.
Condal	Aperient	—	Sodium, 16½.	Sodium, 390½. Magnesium, 27. Ca., 14½. Pot., 4½.	Traces of Alumina, Iron.— Ecole Nat des Mines, Paris.
Contrex- ville (Pavillon)	Alkaline.	Calcium, 3½. Magnesium, ¼.	—	CO ₂ ¾; (Le Cler Spring 10). Traces of Arsenic, Chlorides, Fluorides.	

SPRING.	CHARACTER.	CARBONATES (more or less in form of Bicar- bonates).	CHLORIDES.	SULPHATE.	OTHER CONSTITUENTS AND AUTHORITY.
Evian-les- bains (Cachat)	Alkaline.	Calcium, 1½. Magnesium, ¾.	—	—	CO ₂ and traces of Iron, Magnesium, Sodium, Chlor- ide, Nitrate, Phosphate.
Harrogate	Sulphurous.	—	—	—	—
Hunyadi Janos	Aperient.	Sodium, 8. Strontium, ¼.	Sodium, 15. Calcium, 9.	Sodium, 197½. Magnesium, 195½.	CO ₂ . Trace of Iron.
Leamington	Saline	Calcium, ½ Iron, ¼.	Sodium, 109 Calcium, 5. Mg., 4. Pot., 1.	Calcium, 21½. Magnesium, 11	Lithium, Manganese, Tit- anium, Iodine, Bromine.
Malvern Vide List of Waters	Table.	—	Sodium, 18.	Sodium, 844. Magnesium, 28 Calcium, 17	CO ₂ . Lime Magnesium, Sodium, Chloride, Iodide. (Total = ¾ gr. only).
Rubinat (Llorach)	Aperient	—	—	—	Traces of Alumina, etc.— Bouchardat.
St. Galmier (Romaines)	Table	Calcium, 10. Potassium, 8. Magnesium, 7½. Sodium, 6.	Sodium, ¾. Calcium, ¾. Magnesium, ¼	Calcium, ½. Magnesium, ½ Sodium, ½.	CO ₂ , 20½, Silicates ½, Traces As, P. and I. "Badoit" and "Noel" contain less than "Romaines."
Vichy (average of 3 springs).	Alkaline, Acidulated.	Sodium, 2½. Calcium, ½.	Sodium, ½	—	CO ₂ ½. Traces of K, As., Boric Acid, Fe., Mn. and Mg.
Vittel ('Grande Source ')	Sulphated Ferruginous.	Calcium, 1½. Magnesium Sodium } ¾	Sodium Magnesium } 2. Potassium	Calcium, 4. Magnesium, 3½. Sodium, 3	Traces of Iodine, Arsenic and Iron

BRITISH SPAS AND CLIMATIC HEALTH RESORTS.

Bath.—Climate sedative and relaxing, but invigorating on Downs above city. One of the warmest places in Britain. Mineral springs. Suitable for gout and rheumatism, also for paralysis, neuritis and neuralgia.

Braceborough Spa (LINCOLNSHIRE).—Calcium waters. Beneficial in chronic and obscure toxic conditions and cases of Calcium deficiency, and for eczema and psoriasis.

Bridge of Allan.—Mild and equable. Saline springs. Suitable for catarrhal and hepatic dyspepsia, and "scrofulous" and rheumatic affections. Also in chronic tuberculous affections.

Bulth Wells.—Saline Springs. Beneficial in dyspepsia and constipation, and in catarrhal and chronic tuberculous affections.

Buxton.—Climate peculiarly bracing. Thermal springs. Suitable for gout, rheumatism, chronic tuberculous and catarrhal cases, anæmic and neurasthenic persons and some cardiac cases, including myocardial weakness and high arterial tension.

Cheltenham.—One of the most sheltered and sedative climates in British Isles. Saline springs. Suitable for gout with liver and stomach troubles, hyperacidity, constipation, catarrh of colon, arterial hypertension, glycosuria and obesity.

Clifton.—Bracing and very healthy. Thermal springs. Suitable for chronic respiratory and mild renal affections.

Droitwich.—Fairly equable, remarkable freedom from fog and snow. Brine baths; recommended for fibrositis, neuritis, lumbago, sciatica, rheumatoid arthritis and gout, and in nervous affections, also for traumatic paralysis and atrophies and in neurasthenia and anæmia.

Harrogate.—Tonic and bracing, specially suitable for poor nutrition. Saline-sulphur and chalybeate springs. Suitable for gouty conditions, hepatic inadequacy, constipation, glycosuria, obesity, etc., gouty eczema and other skin affections.

Leamington Spa.—Mild, equable and dry. Saline waters. Suitable for hepatic congestion and enlargement, gouty conditions and tuberculous affections, pelvic congestion, dysmenorrhœa and amenorrhœa.

Lisdoonvarna (CO. CLARE, IRELAND).—Small, sheltered town on West Clare Ry. Climate bracing. Sulphur and Chalybeate springs, suitable for dyspeptic and hepatic disorders, rheumatism and gouty eczema.

Llandrindod Wells—Pleasant and invigorating. Saline and Chalybeate springs. Liver complaints, gout, rheumatism and catarrh.

Llangammarch Wells (BRECON).—Moderately bracing. Saline waters. Recommended for cardiac diseases, Graves' disease, chronic tuberculosis, rheumatism, catarrhal dyspepsia, etc.

Llanwyrtyd Wells (BRECON).—Mountain resort—climate rather humid. Sulphur waters. Scrofulous affections.

Lucan (CO. DUBLIN, IRELAND).—A sheltered spa, nine miles from Dublin. Mild climate. Alkaline Sulphide waters. Chronic rheumatism and gout, psoriasis and eczema.

Mallow Spa (CO. CORK, IRELAND).—Very warm genial climate. Diuretic waters. Suitable in arterial hypertension, rheumatism, and for stimulating metabolism.

Malvern, Great (WORCESTERSHIRE).—Air very pure, bracing, dry and rarified. Summers cool and winters not severe. An unsurpassed hillside health resort. Medicinal waters of the solvent and eliminant class.

Moffat (DUMFRIESHIRE, N.B.).—Climate bracing. Sulphur waters. Rheumatism, gout and skin affections. Indicated for convalescence.

Nantwich and Northwich.—Equable and mild. Brine baths. Indications same as Droitwich.

Strathpeffer Spa (ROSS-SHIRE, N.B.).—Moderately bracing and fairly dry. Thermal waters. Sulphur and Chalybeate. Rheumatism, gout and skin affections. Suited for convalescents and neurasthenics.

Trefriw Wells (CARNARVONSHIRE).—Powerful Chalybeate waters. Suitable for anæmia, chlorosis, rheumatism, neuritis and debility.

Tunbridge Wells.—Climate bracing. Chalybeate waters. Suitable for catarrhal dyspepsia, anæmia and debility. Climate well adapted for phthisis.

Woodhall Spa.—Dry and bracing. Noted for its Bromo-Iodine waters. Rheumatism, neuritis, women's diseases and respiratory diseases. Suited for convalescents and neurasthenics.

MARINE HEALTH RESORTS.

(i.) NORTH-WESTERN GROUP.

Blackpool and Lytham St. Annes.—Climate strongly tonic. Not desirable for invalids in crowded 'season.' Indications (spring and early summer) nervous diseases, convalescence and phthisis.

Colwyn Bay.—Sheltered position—warm and agreeable in winter. Indicated as winter health resort for cases requiring fineequable climate and daily exposure to open air.

Douglas (ISLE OF MAN).—An excellent health resort in spring, early summer and September for delicate persons needing pure marine air with protection against sudden changes of temperature.

Grange-over-Sands and Morecambe Bay.—Pure and sedative air, beneficial to treatment of respiratory affections. A very sheltered health resort for spring and winter months.

Irish Marine Health Resorts.

PORTRUSH.—Fine exposed resort on North Coast with excellent bathing. Equable climate, suitable for neurasthenia, insomnia and convalescence.

NEWCASTLE.—Beautiful resort in Down. Very fine and bracing air.

BRAY AND GREYSTONES.—Facing Irish Sea and protected from westerly winds. Climate dry and bracing.

ROSTREVOR.—Noted for its mild climate. A winter and spring resort for bronchial and pulmonary diseases and for cases requiring rest in invigorating but sedative air.

Llandudno.—Climate mild and bracing. Well suited for patients suffering from chronic maladies of lungs, heart and kidneys, especially in winter.

Llanfairfechan.—A bright and sunny place, fairly warm in winter, cool and bracing in summer.

Oban.—Has a typical, equable West-Coast climate, suitable for convalescents and neurasthenics. Autumn months often very fine.

Penmaenmawr (CARNARVONSHIRE).—Good sands and safe sea-bathing. Climate pleasant in summer and sheltered in winter. Well adapted for convalescence, chest affections, anæmia and neurasthenia.

Rhyl (FLINTSHIRE).—An open breezy resort with extensive sands and good bathing. Very low rainfall. Recommended for children and invalids.

Rothsay (ISLE OF BUTE).—Equable and sedative climate. Winter temperature warmer and summer cooler than average for Scotland. Indicated for catarrhal, heart and kidney affections. Too humid for vigorous persons.

Southport (LANCS.).—A marine winter health resort. Mild, dry and equable. Suitable for convalescence, and laryngeal and pulmonary diseases. Summer atmosphere, extremely clear and exceptionally free from micro-organisms.

(ii.) SOUTH-WESTERN GROUP.

Aberdovey (MERIONETHSHIRE).—The warmest winter resort on the Welsh Coast; sheltered and sunny. Good bathing and river fishing.

Aberystwyth.—Equable and invigorating winter resort. Sheltered from east winds and suitable for phthisis, renal disease and anæmia.

Barmouth.—Winters remarkably mild. Safe bathing on sands. Recommended for bronchitis and phthisis.

Boscastle and Tintagel (N. CORNWALL).—Exposed and picturesque rocky shore. Recommended for respiratory affections but not for rheumatism.

Bude (N. CORNWALL).—A bracing seaside resort, suitable for those suffering from anæmia, debility and brain-fag.

Clevedon (SOMERSET).—A restful and comfortable place on the estuary of the Severn. Sheltered and sunny. Suitable for rheumatism, malaria, renal disease and for old people.

Exmouth (S. DEVON).—Mild and equable. An ideal place for elderly people, those returning from hot countries, and tuberculous children.

Falmouth (CORNWALL).—Climate remarkably equable, more so than any of the health resorts in the South of France or even Madeira. Well suited for chronic phthisis, laryngitis and bronchitis.

Fowey (S. CORNWALL).—Restful health centre, with climate equable, sunny, and sheltered. Well adapted for invalids.

Guernsey.—Mild, without extremes of temperature. More bright sunshine, both winter and summer, than any other part of the U.K. Suitable for phthisis and convalescence.

Ilfracombe.—An invigorating but equable climate, with mild winters. Esteemed for respiratory affections—excepting phthisis,—convalescence and old people, and for those returned from the tropics.

Irish South-Western Resorts.

QUEENSTOWN, GLENGARRIFF, KILKEE and BUNDORAN have sedative and equable climates, suitable for invalids in winter.

Jersey.—Famed for mild, equable and sunny climate. Late autumn and winter specially suitable for elderly and bronchitic subjects. An easily available and good alternative to a sojourn in Algiers or Madeira.

Lynton and Lynmouth (N. DEVON).—Rugged but luxuriant scenery. Pleasantly cool and bracing in summer.

Minehead.—Mild but invigorating; considered beneficial for neurasthenic and cardiac cases.

Newquay (N. CORNWALL).—Mild but bracing, equable climate. Air very good for delicate and “scrofulous” children and early phthisis.

Paignton.—Similar to Torquay but more bracing, and with more wind. Excellent bathing on firm sands. Suitable for delicate persons.

Penzance.—Mild and equable winter climate, suitable for pulmonary phthisis, bronchitis and invalids.

St. Ives.—Resembles Newquay but is more sheltered. Invigorating air excellent for delicate children.

Salcombe (S. DEVON).—Climate one of the mildest in the country. For delicate and elderly persons in winter and spring, also for phthisis and bronchitis.

Teignmouth (S. DEVON).—Mild but bracing. An invigorating and restful summer sea-bathing health resort, well adapted for delicate and elderly persons.

Tenby (PEMBROKESHIRE).—Temperate, mild, insular, and equable in winter, fairly cool in summer. Suitable as winter resort for chronic tuberculous cases and weakly children. Specially recommended for bronchial affections.

Torquay.—Beautifully situated, with mild, soft, equable climate, comparative warmth in winter, cool in summer. Beneficial to chronic pulmonary phthisis, bronchial and cardiac asthma and delicate children.

Weston-super-Mare.—Mild and equable. Well suited for delicate children, for the anæmic and scrofulous and for convalescents—not for rheumatism.

(iii.) SOUTHERN GROUP.

Bognor.—Sunny, South-Coast health resort with firm, dry sands; suited for children and old persons.

Bournemouth.—Mild, fairly dry and equable. Winter resort for phthisis, bronchial diseases and convalescence.

Brighton.—Decidedly bracing. Ideal resort for people run down physically or mentally and for convalescence. Also for children with tuberculous glands.

Littlehampton.—Warm, dry and sunny—more bracing than most South-Coast towns.

Ryde (ISLE OF WIGHT).—Sheltered from S.W. winds and Channel fogs. Well adapted for elderly and delicate persons and for chronic bronchial and pulmonary cases. Exceptionally pure air.

Sandown (ISLE OF WIGHT).—Very sunny and moderately bracing. Early winter months often mild. Good for invalids.

Seaford.—Dry, sunny and rather bracing. Good for children, convalescence, anæmia and early phthisis.

Shanklin (ISLE OF WIGHT).—Mild, dry, sunny climate. Possesses valuable Chalybeate water. Recommended for “scrofulous” and delicate children and for anæmia, debility and chronic renal complaints.

Sidmouth (DEVON).—Winter climate equable, mild and comparatively dry. Suitable for pulmonary phthisis, catarrh and convalescence.

Southsea.—Equable and healthful both summer and winter. Very suitable for delicate children, and for catarrh and chronic phthisis.

Swanage (DORSET).—Climate excellent for delicate children. Indicated at all seasons for chronic phthisis, bronchial catarrh, asthma and pleurisy.

Ventnor (ISLE OF WIGHT).—Mild in winter, cool in summer. Winter climate suitable for pulmonary tuberculosis, "scrofulous" children and bronchial asthma and catarrh.

Weymouth.—Fresh and bracing in summer, equable and warm in winter. An excellent resort for delicate children and for weak and anæmic subjects.

Worthing.—A warm and sheltered climate, and one of the most sunny of the South-Coast resorts. Suitable as winter residence for chronic illness and delicacy.

(iv.) SOUTH-EASTERN GROUP.

Bexhill.—Dry and invigorating climate, suitable for anæmia and convalescence.

Broadstairs.—A quiet, pleasant, sunny resort, well suited for delicate subjects and children in colder months.

Eastbourne.—Climate invigorating, with few local fogs. Sunshine records amongst highest in Britain. Beneficial in anæmia, scrofulous and tuberculous diseases, Bright's disease and convalescence.

Folkestone.—Bracing and fairly dry; cold in spring. Recommended for scrofulous and chronic tuberculous diseases and convalescence.

Hastings and St. Leonards.—Mildness and equability characteristics of winter climate. Suitable for anæmia and tuberculosis and nervous diseases.

Herne Bay.—One of the driest and sunniest climates in England, but exposed to cold winds in spring. One of the most 'healthy' of health resorts.

Hythe.—Both a winter and summer resort. Climate and indications as for Folkestone.

Margate.—Dry and very bracing. Suitable for common types of secondary anæmia and general debility after illness.

Ramsgate.—Dry, sunny and invigorating, and more sheltered than Margate. Winter comparatively warm. Good for early stages of pulmonary tuberculosis and chronic interstitial nephritis.

Southend and Westcliff-on-Sea.—A very real and beneficial 'change of air' for convalescents and delicate children.

(v.) EASTERN GROUP.

Arbroath (FORFARSHIRE).—Dry and invigorating. Good sands, rocks and cliffs.

Bridlington (YORKS).—Invigorating and rather windy climate, suitable in summer and autumn for convalescents.

Clacton-on-Sea.—Dry and bracing; warm and sunny in winter. Suitable for surgical tuberculosis and convalescence.

Cromer and Sheringham.—Very bracing and tonic, but spring is cold. Some forms of pulmonary phthisis, anæmia and convalescence.

Dunbar (FIRTH OF FORTH).—Very bracing; cool in summer. Fine exhilarating air, and sea-bathing. Good for convalescents.

Felixstowe.—Dry, bracing, and very pleasant in autumn. Beneficial in surgical diseases of children, convalescence and incipient phthisis.

Forres (MORAYSHIRE).—'The Devonshire of Scotland'; surprisingly mild and genial. Well adapted for invalids.

Frinton-on-Sea (ESSEX).—Bracing and sunny. Suitable for convalescents and delicate children.

Great Yarmouth.—Pure, bracing air, but with more than average humidity and liability to fog. Excellent for fairly robust subjects.

Hunstanton (NORFOLK).—Invigorating and sunny—well suited for convalescents.

Lowestoft.—Climate bracing and invigorating. Warm and pleasant summer and autumn resort. October to December often bright and dry. Suitable for convalescence, 'malnutrition, and early phthisis.

Montrose (FORFARSHIRE).—Pure, clear and invigorating air. Well suited for quiet recreation and repose.

Mundesley (NORFOLK).—Bracing and tonic. Well suited for all conditions requiring invigorating air.

Nairn (N.E. SCOTLAND).—Cool and bracing summers and relatively warm winters. Atmosphere remarkable for its transparency. Well suited for chronic catarrh and delicate persons.

North Berwick (FIRTH OF FORTH).—A sunny place, especially beneficial for 'after-cure' of spa-goers and convalescents.

Peterhead (ABERDEENSHIRE).—Winters milder than might be expected. Dry, bracing air, invaluable for nervous diseases.

St. Andrews (FIFE).—One of the most bracing climates in Gt. Britain.

Saltburn-by-the-Sea (YORKS).—In the valley the climate is mild, moist and sheltered, but dry and bracing on the cliffs. Recommended for rheumatic and arthritic affections, neurasthenia and early phthisis.

Scarborough.—Summer climate suitable for rickety children, anæmia and convalescents. Two mineral wells—saline and chalybeate.

Walton-on-the-Naze.—Easterly marine air very good for young people and convalescents.

(vi.) INLAND HEALTH RESORTS.

Braemar (ABERDEENSHIRE).—A Highland sub-alpine climatic resort, indicated for convalescence and neurasthenia.

Church Stretton (SHROPSHIRE).—An 'after-cure' station of great natural beauty, with bracing, invigorating climate.

Crieff (PERTHSHIRE).—Mid-way between East and West Coasts, and surrounded by fine glens and hills. Climate of intermediate character, suitable for after-cure.

Crowborough (SUSSEX).—Equable and bracing. Suitable for respiratory diseases, neurasthenia, anæmia, debility and convalescence.

Dunblane (PERTHSHIRE).—The 'Gate of the Highlands.' Sheltered from cold winds and with mild and equable climate, even in winter.

Grantown-on-Spey and Aviemore (INVERNESS-SHIRE).—One of the most remarkable health resorts in the country. Semi-alpine climate, tonic and sedative, with powerful restorative effect in nervous diseases.

Hindhead (SURREY).—Picturesque common and open moorland, with dry and very bracing climate, specially suitable for delicate children.

Ilkley (YORKS).—Close to moors, 750 ft. above sea-level. Bracing and invigorating. Beneficial in chronic gout and rheumatism.

Matlock Bank and Matlock Bath (DERBYSHIRE).—Matlock Bath has natural sub-thermal waters useful in gout and rheumatism. Climate mild and equable.

Peebles (PEEBLESHIRE).—Comparatively dry and bracing. Cold in winter. Natural saline waters. Recommended for neurasthenia, convalescence and as 'rest-cure.'

Pitlochry (PERTHSHIRE).—In centre of Scottish Highlands. Beautiful and historic scenery. Air fresh, bracing and cool in summer. Suitable for convalescence and 'after-cure.'

For further details see Treatise by R. Fortescue Fox in the "Medical Directory" 1929 (J. & A. Churchill, London), from which the above notes have, in the main, been abstracted.

For a good treatise on the subject, beautifully illustrated, see "HEALTH RESORTS OF THE BRITISH ISLANDS," by Neville Wood.

Advantages of British Health Resorts for Foreign Invalids.

Hitherto the movement of invalids has been in one direction only. Value of our climatic conditions and maritime resorts.—Neville Wood, *Int. Cong. of Med.*, 1913.—*B.M.J.* ii./13,542; *L. ii.*/13,809.

Spa treatment in the British Isles—Special Numbers.—*Pres.*, March, 1921, 1924, 1926 and 1928.

MILK ANALYSIS.

Average Chemical Composition of Milk of good quality :—

For some years past we have given the following figures, which we consider are still representative :—

	Per cent.
Water	87.75
Fat	3.50
Casein	3.20
Sugar	4.40
Albumin	0.40
Ash	0.75
} Solids-not-Fat	
} 8.75	

As averages from 330,000 analyses conducted during 20 years by the Aylesbury Dairy Company, the following are quoted by Richmond :—

	Per cent.
Water	87.34
Fat	3.75
Casein	3.0
Sugar	4.7
Albumen	0.4
Ash	0.75
Other constituents	0.06

The figures are varied by other workers, some suggesting 3.9% fat as an average. Dairy farmers, however, with the sole object of milk production, as distinct from 'dual purpose,' bring up the average by milking selected types of cows, such as the Jersey breed. Jerseys may give as high as 8% (E. F. Sage). Blyth gives a table showing variations with different breeds.

'*Certified Milk*' examined in the author's laboratory 26/3/29 showed 3.93% fat and 8.83% solids-not-fat. (Sp. Gr. 1.033.) '*Household Milk*' examined on the same occasion showed 3.44 and 8.42% respectively (Sp. Gr. 1.032). Two other samples showed 3.24 and 8.45, and 3.3 and 8.57%.

Milk also contains small quantities of Citrates and Emzymes.

Two substances are present which, in the presence of Acetic Aldehyde, can exert reducing and oxidising properties respectively.—Paul Haas and T. G. Hill, B.P. Conf., 1923; P.J. ii./23,94.

The following data are necessary to determine quality of a specimen :—

- (1) **Specific Gravity** may be determined by a Specific Gravity bottle or Lactometer; the average reading is 1.031.
N.B.—Low gravity may indicate added water, or in some instances richness in fat.
- (2) **Total Solids.** Evaporate 5 Gm. of the specimen on a water bath in a tared platinum capsule; the residue, which should be nearly white, averages 12.8%. Minimum: 11.5%.
- (3) **Fat.** Many different processes are in use for this important determination, and of these the Werner-Schmidt and Gottlieb methods are convenient for rapid estimations, but a modified Adams extraction method is preferred when greater accuracy is required.

Werner-Schmidt Method. Take 10 Cc. of the milk in a 50 Cc. tube, graduated in tenths of a Cc., and 10 Cc. of Hydrochloric Acid, and boil with shaking until the liquid turns dark brown. Cool rapidly in water and add 30 Cc. Ether, shake vigorously and allow to separate. Read off volume of Ether and by means of a pipette transfer 10 Cc. to a tared beaker. Evaporate Ether, dry at 100° C. and weigh. In preference, for accurate work, exhaust the contents of the tube with several quantities of Ether and weigh the whole.

Gottlieb Method. 10 Cc. of milk is shaken with 1 Cc. of 0.96 Ammonia, 10 Cc. of Alcohol and 25 Cc. of Ether. Petroleum Ether, 25 Cc., is added, and from the layer of about 50 Cc. an aliquot portion is removed, evaporated and weighed.

Extraction Process (Adams). 5 Cc. of sample is run from a pipette on a strip of "fat-free" filter paper and allowed to dry. This is then rolled up, dried at 100° C., and extracted with pure dry Ether for 5 hours in a Soxhlet apparatus. The Ether is distilled off, and the fat weighed, after drying at 100° C. for about 20 minutes. There are various modifications of this. Babcock, for example, evaporates with Asbestos prior to extraction.

Legally the content must not be less than 3%.—*Sale of Milk Regulations 1901 (under Sale of Food and Drugs Act, by Board of Agriculture. See p. 491 & 492). Applies to Gt. Britain.*

(With regard to this 3% Milk Fat Standard it is known that the yield from the same cow may vary greatly, e.g., it may be 2½% in the morning and as high as 4½% in the afternoon. The milking should be done at equal 12 hour intervals as far as possible.)

Cream in normal milk is about 10%, varying with season, pasture, etc.

Milk that has been adulterated with water throws up its cream readily.

(4) Non-fatty Solids.

Are determined by subtracting the fat content from the Total Solids. For the purposes of the Sale of Food and Drugs Act they **must not be less than 8.5%**. Sale of Milk Regulations 1901: "or until the contrary is proved it shall be presumed that the milk is not genuine by reason of abstraction therefore of milk-solids other than milk-fat or by the addition of water."

Only 2.19% of samples of mixed milk of a herd of cows, as kept in this country, are likely to fall below 8.5%, and in only 0.3% are they likely to be below 8.4%.

A milk should never be pronounced as watered on the evidence of solids-not-fat alone, **unless this is well below 8%**: determination of Milk Sugar, total Nitrogen and Ash, should be made in addition; a judgment formed on the three determinations will probably be correct, and if the figure for at least two are above the limit the milk is probably genuine.

Out-door and indoor feeding.—It is not possible to state the differences due to these, but it is a well-known fact that there is a greater yield of milk when cows go on grass, but the milk is poorer.—Richmond.

Variations in the composition of Milk.—By J. F. Tocher, H.M.S.O., Edinburgh, 1925.—quoted by Richmond.—

When the Government figures were laid down, the authorities had no real scientific basis on which to decide what the minimum percentages should be from herds of various sizes and the present presumptive standards are suitable only in the case of bulked milk from many cows, i.e., these standards are useful and valid only in the case of bulked milk in large cities.

12% of all samples from individual cows fall below the fat standard and 24% below the solids-not-fat standard.

The percentages of fat and solids-not-fat in a sample of commercial milk depend upon several factors, one of the most important being the number of cows whose mixed milk is represented in the sample. If the sample was, e.g., from 100 cows, one would be quite certain that the milk would be always above the standards.

Cows of three years of age give a higher proportion of solids-not-fat than cows of 10 years of age—and the same is true of fat, and the percentages of these constituents vary with the number of weeks the cow has been in milk.

The percentage of Lactose falls during the lactation period, but is greater with increased yield of milk. The percentage of Albumin rises during the lactation period. If a sample of milk contains a high proportion of Lactose, say 5.5%, then the proportion of Albumin is low—0.095%, but if Lactose is 3.17%, the Albumin is 0.15%.

(5) Lactose (Milk Sugar). Average content 4.4%.

The percentage content falls during the lactation period, but is greater with increased yield of milk.—Tocher.

The sugar can be determined by a volumetric or gravimetric estimation of

its Copper-reducing power after removal of proteins and fat. This is best effected by diluting 25 Cc. of the milk to about 400 Cc. in a 500 Cc. graduated flask and adding 10 Cc. of Fehling's Copper solution and 35 Cc. N/10 Sodium Hydroxide. After shaking thoroughly and adjusting to the mark the liquid is filtered through a dry paper, 50 Cc. of the filtrate being used for the determination.

A more convenient and rapid process is that of H. D. Richmond (Anal., '25, 17). 10 Gm. of milk are weighed into a 100 Cc. graduated flask, diluted with 50 Cc. of distilled water and 10 Cc. of Mayer's Reagent, and 2 Cc. of N/1 Sulphuric Acid added. The whole is well shaken, diluted to 100 Cc. and filtered. After neutralising 25 Cc. of the filtrate to Phenolphthalein (1 drop used), 20 Cc. of N/10 Iodine solution and 30 Cc. N/10 Caustic Soda solution are added. The mixture is allowed to stand for 20 minutes and after the addition of 4 Cc. N/1 Sulphuric Acid the excess of Iodine is titrated with N/10 Sodium Thiosulphate.

%Lactose ($C_{12}H_{22}O_{11} \cdot H_2O$)

$$= \text{Cc. N/10 Iodine used} \times 0.072 \times \frac{100 - (0.3 + \text{Fat} \times 1.1)}{\text{wt. of milk taken.}}$$

Lactose Determination by Polarimeter:—

Add to 60 Cc. of the Milk 10 Cc. of a solution of Mercury in twice its weight of Nitric Acid 1.43 diluted with four times its volume of water. Make volume up to 102.4 Cc., filter. Note rotation in 200 m.m. tube,—divide by 2 and by 53 the specific rotation for lactose. Result is the amount of lactose per Cc. in the solution. Multiply by 100 to give the amount in 60 Cc.

Mineral Matter of milk can be obtained by igniting the milk solids, and usually averages 8.3% of them.

N.B.—A dilution of normal milk with water will reduce the ash almost proportionately to quantity of water added, so the combination of a low ash and low non-fatty solids point strongly to addition of water.

The Salts in human and cow's milk vary very greatly. Nearly $\frac{1}{2}$ of the salts of cow's milk are alkali citrates and alkali earth citrates. Human milk contains 0.5 Gm. of Citric Acid as citrates, whilst cow's milk contains from 1 to 1.5 Gm. per litre.

(6) **Casein Estimation** (Average content 3.2%).—Dilute 20 Cc. of the sample with 300 Cc. water, and add strong acetic acid drop by drop to complete precipitation. Pass in carbon dioxide for 20 minutes, collect the casein and fat on a weighed filter paper; wash thoroughly with, firstly, alcohol, then ether to remove fat (well conducted in a Soxhlet thimble on water bath), dry and weigh.

Many proteins are precipitated by Acetone. Weyl applied this property to estimation of the Proteins in cow's milk and in fresh bullock's blood and obtained concordant results. The milk or blood is diluted with equal volume of water and poured into four volumes of Acetone. The precipitate is collected, washed with equal volumes of Acetone and Water then with Alcohol and is finally extracted with Ether in a Soxhlet apparatus, dried and weighed.

Lecithin contained in various milks. Human, average, 0.0499%, cows' 0.0629%, asses' 0.0165%. See also *Lecithin Chapter*.

The **Average Constituents** of good milk (as stated at the commencement of this chapter) are **affected by the addition of water** as follows:—

Genuine Milk.			
Percentage of Fat	3.50
Solids-not-Fat	8.75
Milk" with added Water.		Fat.	Solids-not-Fat.
95% milk, 5% water	3.32 8.31
90% milk, 10% water	3.15 7.87
85% milk, 15% water	2.97 7.43
80% milk, 20% water	2.80 7.00
75% milk, 25% water	2.62 6.56

Various forms of apparatus are in the market for detecting adulterations of milk, *e.g.*, The **Lactometer Cream Tube** and **Lactoscope**—the last mentioned detects by the optical properties of milk its adulteration with water—or removal of cream.

COLOSTRUM.—The milk from mammals shortly after birth of their young differs from normal milk in containing a very high percentage of an albumin closely resembling blood albumin. The proteins it contains are soluble.

Colostrum provides readily absorbable nutriment, as the infant's stomach contains no gastric juice at the commencement. It is highly laxative in properties, probably owing to its high fat content.

The fat content of the fæces of the infant is always high—ranging from 10 to 20%—during the first week it is as high as 40 to 50%.

Cow's milk contains about twice as much **Phosphatide** as human milk, the amount being higher with a milk or cream with a high percentage of fat, though there is no parallelism between the fat and Phosphatide content. Milks containing a considerable amount of Colostrum also show a high Phosphatide content. The total Phosphorus of cow's milk averages about 4 times that in woman's milk, and is still higher in goat's milk.—Jl. Biol. Chem., per Jl.A.M.A. ii./25,775.

The proteins of Milk consist almost entirely of Casein and Albumin. Analyses show mean percentages as follows:—

		Casein ('Lactalbumin.')	Albumin.	Maximum	Minimum
Cow's Milk	..	6	1	7 to 1	4.5 to 1
Goat's	3	1	3 to 1	2 to 1
Sheep's	3	1	4 to 1	3 to 1
Mare's	1.5	1		
Asses'	1	2.3		
Human	1	1		

The proportion of these two forms of Protein is adjusted to the needs of the animal, the albumin being easily digested, and the casein digested with difficulty. A sixteen pound infant requires more casein than one weighing 12 lbs. though of the same age, and the human milk changes accordingly. More and more casein and less and less albumin is required by the child as time goes on. cf. Whey Powder, Vol. I., p. 588.

The milk supplied in this country in a large proportion of cases is from cows in calf. That from cows not in calf is more digestible, as the drain of the embryonic calf interferes with quality of the pregnant cow's milk.

(7) **Albumin Estimation.** (Average 0.4%)

Various methods are used. The following of Ritthausen (mentioned by Blyth) is simple. Dilute 10 Gm. of milk with 90 Cc. of water at 42° C. Add 1.5 Cc. 10% Acetic Acid. Casein settles in 5 minutes. Albumin remains in solution. The precipitated Casein is treated with Alcohol and Ether and may be weighed. Neutralise the filtrate with NaOH, add 3 Cc. of 10% Acetic Acid, boil 15 minutes and collect on a filter or a Kjeldahl may be conducted, multiplying the N by 6.38. Diminished content below 0.41 to 0.45% may be useful to show adulteration.—See Blyth, p. 250.

Skimmed or Separated Milk.—An Amendment in 1912 of the Sale of Milk Regulations replaced the limit, which had been previously 9% total solids, by one of **8.7% milk solids, other than fat.** This extends to England and Wales.

Taking advantage of the exceedingly low standards laid down by the Board of Agriculture it appears that milk has been or is toned down with skimmed or separated milk so as to keep the fat content **just within the standard.**

The milk must be labelled (under the Milk and Dairies Act, 1915) '**Machine-Skimmed Milk,**' or '**Skimmed Milk.**'

A RÉSUMÉ OF VARIOUS ACTS OF

PARLIAMENT, REGULATIONS, AND OFFICIAL PUBLICATIONS

MILK AND DAIRIES (CONSOLIDATION) ACT, 1915. (*Does not extend to Scotland or Ireland.*) *To come into force one year after the termination of the war. Actually came into force September 1, 1925.*

Section 1.—Gives the Local Government Board powers to make Orders for Registration of Dairymen, Inspection of Cattle, Dairies, and Milk Stores, for the use of the Designation '**Certified Milk,**' and allied matters.

Section 3.—Gives M.O.H. power to stop the supply of milk from a dairy which has caused, or is likely to cause, tuberculosis.

Section 4.—Entails on the local M.O.H. to trace the source of supply of tuberculous milk, and to give notice to the County M.O.H., who shall then cause the cattle in question to be inspected.

Section 5.—Any person selling or allowing to be sold, or uses or allows to be used in the manufacture of products for human consumption the milk from any cow which has given tuberculous milk, or is suffering from emaciation due to tuberculosis, or inflammation of the udder, or diseases specified (acute mastitis, actinomycosis of the bladder, anthrax, foot and mouth disease, and suppuratation of udder) is guilty of an offence under the Act, if he had previously received notice, or otherwise knew, or with ordinary care should have ascertained that the cow was giving tuberculosis milk.

Section 8.—Allows L.G.B. Inspectors, M.O.H.s, etc., to take for examination samples of milk at any time.

Section 10.—A local authority *may* appoint one or more veterinary inspectors for the purposes of the Act, and *may* provide or arrange for facilities for bacteriological or other examinations.

Section 12.—Allows Sanitary authorities to maintain depots for the sale of milk at not less than cost price, specially prepared for consumption by infants under two years, and provide laboratories, plant, etc.

It would appear therefore that the onus of carrying out the provisions of the Act falls on the shoulders of the local M.O.H. There is no provision in the above Sections for routine periodic inspections.

Milk and Dairies Order, 1926, made under the Milk and Dairies Consol. Act, 1915. Came into operation October 1, 1926.

S. R. & O., 1926, NO. 821.

Section 1 et seq.—Refers to Registration of Dairies, Cowsheds, etc.

PART IV.—*Health and inspection of cattle.*

Section 8.—Every county and county borough council shall cause such inspections of cattle to be made as may be necessary and proper for the purposes of the Act.

Section 11.—Veterinary Inspectors to serve a notice stopping supply of milk from cows suffering from : any comatose condition, any septic condition of the uterus, any infection of the udder or teats likely to convey disease **in addition to the diseases specified in Section 5 of the Act. (q.v.)**

PART V.—*Provisions for securing cleanliness of dairies and protecting milk against infection.*

Sections 17, 18, 19.—Prevent the sale of milk by persons suffering from, or from premises where there are persons suffering from, infectious disease.

NOTE.—*Inspections are only to be carried out 'when necessary for the purposes of the Act,' i.e., after tuberculous milk has been found exposed for sale.*

MILK AND DAIRIES (AMENDMENT) ACT, 1922. *Came into operation September 1, 1922.*

This Act postponed for a further period the Milk and Dairies (Consol.) Act, 1915 (*v. antea*).

2.—Gives local authorities power to refuse registration of, or remove from register, retailers of milk likely to endanger the public health.

5.—No person shall sell or offer or expose for sale the milk of a cow suffering from tuberculosis of the udder, and in the event of his so doing he shall be liable to a fine on first offence of £20, and for second and subsequent offences to a fine of £100 or 6 months' imprisonment or both.

NOTE.—*Section 5 of this Act places the responsibility on the purveyor of the milk.*

Milk (Special Designations) Order, 1923, made under the 1922 Amendment Act. Came into operation July 1, 1923.

S. R. & O., 1923, NO. 601.

3.—The special designations under which milk may be sold are : (1) 'Certified'; (2) 'Grade A (Tuberculin Tested)'; (3) 'Grade A' and (4) 'Pasteurised.'

6.—In the case of 'Certified' or 'Grade A (Tuberculin Tested)' milks the producer must possess a vet's. certificate showing the results of an examination carried out **not more than three months before** and a certificate of a prescribed Tuberculin Test carried out within a similar period, and in the case of 'Grade A' milk a vet's. certificate of examination of Milk cows carried out **not more than one month before**. Licences to be renewed yearly.

THIRD SCHEDULE.

PART I. Conditions subject to which licences for selling milk as 'Certified' are granted.

Producers to have every animal examined and submitted to T.T. every six months. No animal which has not passed the T.T. shall be added to the herd. Animals reacting to be removed from the herd. Complete register of animals to be kept. The herd to be completely isolated from all other cattle. *The milk must be bottled on the farm immediately after production.*

PART II. Provides the conditions subject to which licences for selling milk as 'Grade A (T.T.)' are granted.

The milk shall not at any stage be treated by heat.

PART III. Conditions, etc., for selling milk as 'Grade A.'

No reacting animal shall be in the herd. Milk cows to be examined every three months. Diseased animals to be removed from the herd immediately. If tubercle bacillus is found in the milk the producer shall remove diseased animals from the herd and inform the licensing authority how the animals have been disposed of. Complete register of cows to be kept and cows in milk in the herd to be kept separate from all other cows in milk.

The milk is not to be treated by heat at any stage, unless a licence to sell such milk as Pasteurised has been granted.

ORDERS APPLICABLE TO SCOTLAND.

Milk (Special Designations) Order Scotland, 1923.—S. R. & O., 1923, NO. 656/S.42, and the **Milk (Special Designations) Amendment Order Scotland, 1923.**—S. R. & O., 1923, NO. 869/S.55.

These Orders have essentially the same objects as the Order for England and Wales. They are issued by the Scottish Board of Health.

Milk and Dairies (Scotland) Act, 1914. Came into operation 1st September, 1925.

3.—Every local authority may appoint a qualified Veterinary Surgeon to act as an inspector under the Act, and may make arrangements for the bacteriological or other examinations of samples.

4.—*The M.O.H.* or Sanitary Inspector shall inspect every **dairy** in the district **at least once a year**, and the **Veterinary Inspector** shall inspect the **cattle** at least **once a year**, and these authorities have power to examine cattle and dairies in other districts consigning to their own district contaminated or impure milk.

5.—The local authority has power to authorise inspection of premises or examination of cattle of occupiers, not dairymen, who sell milk in small quantities to employees or neighbours.

7.—It is unlawful for a person to trade as a dairyman without a certificate of registration from the local authority.

9.—It is the duty of every local authority to make by-laws :—(1) for inspection of cattle in dairies; (2) for prescribing the structure and cleansing

facilities of dairies; (3) for the prevention of impurities in milk; (4) for prescribing precautions against infection or contamination of milk.

10.—The Local Government Board may require enforcement of the Act by local authorities.

11.—If a local authority believes that **another district consigning milk to its own** is not carrying out the provisions of the Act it may complain to the L.G.B.

12.—The Board may make Orders concerning measures for cooling milk and protecting it against infection or contamination, for the prohibition of colouring matter or addition of other substances, for the manner of conveyance of the milk, and for the labelling of receptacles.

13.—**No person shall sell milk from a tuberculous cow or from a cow suffering from infectious disease.**

14.—Dairymen must give notice to the authority of any tuberculous or infected cows, or (15) of any infectious disease of persons on the premises, and (17) persons so infected must not assist in the dairy.

20.—Where there is an outbreak, or a liability of an outbreak, of infectious disease, or where milk supplied is contaminated or impure, the local authority may require the dairyman, whether within or without the district, to give a complete list of the names and addresses of all his customers and of the sources from which he obtained the milk.

21.—Authorities shall have power to take samples of milk.

22.—A Veterinary Inspector may apply to any cow in any district the Tuberculin or other test to discover whether a cow has tuberculosis.

27.—A **warranty** or invoice **shall not be available as defence** in respect of milk.

28.—Local authorities may establish depots for sale of milk for consumption by infants under 2 years.

These regulations seem to be more stringent than those of the English Act.

Designated Milks.

The **Grade A** milk is superior to the ordinary milk of the country, and is reasonably safe. Nos. (1) and (2) are superior to (3).

The **Tuberculin Test** is to be done at 6 month intervals. Reactors are to be removed forthwith. Combined subcutaneous and ophthalmic tests of cows are required in respect of herds supplying tubercle-free milk.—B.M.J. i./25,409. (*Vide Intradermal Test—infra for latest recommendation.*)

Certified Milk (the highest grade) is produced under similar conditions to the above, but is to be bottled on the farm immediately after production. The cap is to bear name and address of producer, date and the words 'Certified Milk.'

Results show that it is possible to maintain the Ministry's standard for certified milk, and that clean milk production rests not so much on buildings and equipment as on the skill of the workers and the interest of the farmer or milk dealer.—R. S. Williams, B.M.J. ii./26,242.

Pasteurised Milk under the Order must be submitted to a temperature of not less than 145 or more than 150° F. for at least $\frac{1}{2}$ hour and immediately cooled to 55° F. or lower. 'Flash' methods are not allowed.

Bacteriological Standards.

CERTIFIED.—30,000 maximum bacteria per Cc., and no Coliform bacillus in 0.1 Cc.

GRADE A.—200,000 maximum bacteria per Cc., and no Coliform bacillus in 0.01 Cc.

GRADE A. MILK PASTEURISED.—Not more than 30,000 bacteria per Cc., and no Coliform bacillus in 0.1 Cc.

PASTEURISED.—Not more than 100,000 bacteria per Cc.

Technique in Grading Milk.

Precise instructions to get uniform laboratory methods are given in a Circular issued by the Ministry of Health, Jan. 13, '23.

With regard to Veterinary Examinations, Memorandum 77/Foods, Jan. 1923, prescribes as to the Tuberculin Test.—L. i./23,296.

Tuberculin Tests in Cattle with special reference to the Intradermal Test. MEDICAL RESEARCH COUNCIL, SPECIAL REPORT SERIES, No. 94, H.M.S.O., 1925.

The Subcutaneous Test is satisfactory under laboratory conditions, but not under farm conditions. The **Intradermal Test** is superior, while the **Ophthalmic Test** must be regarded as a **subsidiary test**. The percentage of error with the Intradermal Test is small; animals diagnosed as tuberculous by this test have not shown tuberculosis on naked-eye examination *post mortem*, but have been proved tuberculous by microscopic examination and guinea-pig inoculation. The test has the advantages over the Subcutaneous Test that temperature observations are not required, that the animal need not be kept at rest, that it does not interfere with farm routine, that only three observations are usually necessary, that a smaller quantity of Tuberculin is needed, and that the technique is easily acquired. 'Old Tuberculin' (either bovine or human strain) is used; it must be of proved high potency and is given undiluted. In combining the Ophthalmic Test with the Intradermal Test frequent examinations of the animal's eyes are necessary as the reaction when positive is apparent 24 hours after the second instillation.

Modified Intradermal Test.

A further report **The Intradermal Tuberculin Test in cattle**—J. B. Buxton and A. S. McNalty, Med. Res. Council, Spec. Rept. Series, No. 122, 1928) by the Tuberculin Committee of the M.R.C., states that the Intradermal Test is more trustworthy. It involves two injections of Tuberculin—a '**sensitising**' and a '**reacting**' dose—on different occasions. Can be readily performed under farm conditions, has little or no effect on milk yield and is free from risk in pregnant cows and young animals. Ophthalmic test unreliable.—B.M.J. ii./28,808.

The prices of the various grades of milk in London (1929) were as follows:—

				WINTER PRICES.		SUMMER PRICES.	
				QUART.	PINT.	QUART.	PINT.
Certified Milk	1/1½	8d.	1/-	7d.
Special Nursery Milk	11d.	6½d.	10d.	6d.
(From Grade A farms of Tuberculin-tested cows and Pasteurised.)							
Grade A Pasteurised	9d.	4½d.	8d.	4d.
Household Milk	7d.	—	6d.	3d.

The Tuberculosis Order, 1925. *Came into operation September 1, 1925.*

S. R. & O., 1925, No. 681.

Sections 2, 10, 11.—Any person having a cow which appears to be suffering from tuberculosis of the udder or any chronic disease of the udder, or from tuberculous emaciation, or from chronic cough and showing definite clinical signs of tuberculosis immediately to give information to a police-constable or an inspector, and must isolate the animal and keep the milk separate.

Section 4.—A Veterinary Inspector may enter at any time and examine animals and require any cow to be milked and take samples of milk.

Section 5.—Where the Inspector's report shows the animal to be suffering from tuberculosis, the local authority must immediately notify the owner to **slaughter the animal**.

REMARKS:—*If the Ministry of Health enforced all the above Rules and Regulations more vigorously, it would undoubtedly lead to a considerable reduction in bovine tuberculosis, but the weakness of the whole of the legislation seems to be concerned with the work of the Inspectors.*

The milk supply and its improvement.—W. G. Savage, L. i./25,1095,1146, 1199,1313,1360.

Clean Milk.

Milk falling below Grade A standard is an article so damaged that it cannot be regarded as satisfactory. If the producer disregards the necessary requirements (as to clean milk), he saves about ½d. per gallon, and saves a further 2d. per gallon by omitting to ensure that his herd is healthy. **Not for**

many years to come will the bulk of the milk supply be produced from tubercle-free herds, but production of milk of decent cleanliness is practicable. If the producers of the country want to do it, and the public demands it, the entire milk supply can soon be raised to Grade A, and all milk should be of that standard, whether consumed raw or pasteurised.—W. Buckley (National Clean Milk Society), B.M.J. ii./25, 249. *Of the 2,500,000 milk cows in this country 1,000,000 are tuberculous* *ibid*, 253.

Although many Orders have been passed safeguarding the health of cows in, cowsheds, the only Order which would be of any real service would be one **to abolish cowsheds altogether**. It is only through open-air life and healthier conditions that tuberculosis is disappearing in human beings and this applies to cows, whose proper environment is the open field. The cowshed is the breeding-place of organisms. During the years 1920-24, of **16,249 cows slaughtered in Edinburgh 7,277, or 44.8%, were tuberculous**. In one city in Lancashire of 2730 cows taken from cowsheds and slaughtered, 10.37% were wholly or partly tuberculous. Only by giving cows an entirely open-air and free life shall we secure an abundant, clean, cheap, and safe supply of milk.—W. G. A. Robertson, Pr., June, '27, 365.

We fear it is only too true as remarked by H. M. Cargin (B.M.J. ii./21, 894) that Graded (Tuberculin Tested) Milks only provide increased immunity to those who can afford them.

The nomenclature of the grades is very misleading. There is no doubt that *Grade A*, which is only *the third of the qualities* is considered by many people to be the *first quality*, while the Tuberculin-Tested milk has not its proper position in the public mind because of the confusion of Grade A milk with that of the highest quality. There should be a revision of the nomenclature. Licensed graded milk still amounts to little more than 1% of the total milk used in Scotland. The liability of ineffective pasteurisation causes this to be a danger rather than a help by misleading people as to its safety. In view of the propaganda being carried on by the Empire Marketing Board for increased consumption of milk, it would be a good thing if the Minister of Health could reassure the public mind as to the quality of the milk.—Drummond Shiels (Parl. Notes), L. ii./28, 306.

Pasteurisation.

Notes on the Pasteurisation of Milk.—J. M. Hamill, Min. Health Reports on Public Health and Medical Subjects, No. 17, H.M.S.O., 1923:—

From the public health point of view the term 'Pasteurisation' should be confined to the process of heating milk to **not less than 145°F. and not more than 150°F. for 30 minutes** and experience shows that this properly carried out is sufficient to destroy virtually **any pathogenic organisms** without producing appreciable change in the physical and chemical characters of the milk. *B. tuberculosis*, *B. diphtheriae*, *B. dysentericus*, *B. typhosus* and other organisms of the *typhoid-paratyphoid* group, together with the virus of foot-and-mouth disease, are **all destroyed** by pasteurisation. Under certain conditions a **small proportion(!) of tubercle bacilli** may escape actual destruction, but their virulence is so impaired as to make them harmless. Some strains of streptococci may survive, but not those believed to be responsible for septic sore throat. Pasteurisation therefore affords a simple means of rendering milk reasonably safe as regards risk of transmitting disease. Pasteurisation does not destroy all the **non-pathogenic** organisms, though their number may be **reduced by 99%**. The sporing organisms and a small proportion of Lactic Acid bacteria survive. The great **reduction in Lactic Acid bacteria**, enabling milk to keep fresh longer, is the chief advantage which pasteurisation offers from the commercial point of view. Generally speaking, the number of bacteria in milk after pasteurisation is greater in milk which contained a large number of bacteria before pasteurisation than in milk which originally contained relatively few bacteria—this is of practical importance, as the bacterial content of pasteurised milk gives an indication of the bacterial content before pasteurisation.

There is no appreciable change in the physical and chemical characteristics of properly pasteurised milk. When milk is pasteurised at 145° F. for 30 minutes the 'cream line' is hardly affected, but at 148° F. it may be decreased

by 40%—the integrity of the 'cream line' is important commercially. Pasteurisation causes **no appreciable change in the milk proteins**, but at 150° F. about 5% of the milk albumin is rendered insoluble. Pasteurisation does not cause the soluble Calcium and Magnesium Phosphates to separate out, and has only a slight effect on the enzymes. Vitamins A and B are unaffected, but Vitamin C is destroyed.

The ideal milk supply would of course be milk obtained from perfectly healthy cows under the cleanest conditions, consumed immediately with the least possible manipulation, but in a highly urbanised country such as England this is impossible and without some process for preserving the keeping quality of milk a proportion of the population would be forced to curtail or even do without a very important food. By subjecting the average milk of this country to pasteurisation the destruction of any pathogenic organisms is virtually assured and its keeping qualities are improved.

Experimental evidence does not bear out the assertion that bacteria grow faster in pasteurised than in raw milk—the rate of bacterial increase is approximately the same. It is alleged that pasteurisation will encourage dirtiness in milk production, but this is not so, as milk so stale as to be unfit for sale will not have its flavour improved by pasteurisation—moreover, only a milk sufficiently clean before pasteurisation would comply with the requirements of a bacterial count after pasteurisation.

The **nutritive qualities of milk do not appear to suffer appreciable change from pasteurisation, according to the Report, except in respect of anti-scorbutic property** which can be corrected by orange juice. It is held by some that changes referred to in the physical and chemical characters are indicative of possible subtle alterations in nutritive value, not easily detected or estimated, which are perhaps of far-reaching importance. Even assuming, however, some depreciation of these hypothetical nutritive values, it is not unreasonable to assume that the impairment would be of the same order as in those characteristics capable of observation, *i.e.*, partial and slight impairment rather than complete destruction, and from a practical standpoint the positive advantages of pasteurisation outweigh any possible slight depreciation of nutritive elements, the existence of which is hypothetical. Extensive experience of feeding children on pasteurised milk shows it to be as well borne by them as raw milk and (except in anti-scorbutic property) equally nutritious.

Description of Pasteurisers "Flash"—this type has disadvantages, and is not adequate to ensure definite results. **Retarders**.—The same remarks apply to these. **Holder**.—Large containers working automatically with a Time Temperature Recorder. These are well spoken of in the Report.

Extent of reduction of bacteria.—The Pasteurising process has a remarkable power in reducing the bacterial content. According to notes in our possession a content of 250,000 to 300,000 organisms per Cc.—with 800 to 1,200 coliforms per Cc.—in raw household milk is reduced to 6,000—9,000 per Cc. and nil in 1/10 Cc. respectively in half an hour. The science of Pasteurisation has been so perfected that a **positive result** in the matter of coliforms in Pasteurised milk is regarded as **evidence of the careful cleaning of the plant** and efficient operation generally. There is no evidence to suggest that coliforms from a bovine source have a significance which generally attaches to the presence of coliforms in a water supply.

Pasteurisation of Milk in New York City is accountable, according to Dr. Charles E. Worth, for the reduction of the death-rate of infants under one year from 165 per 1,000 born to 70 per 1,000 born.—M.P.C., Oct. 25/22, 343.

Public Health Report on the effects of using fresh milk and various forms of preserved, reconstructed, pasteurised and dried milks, with a study of their vitamin value.—J. M. Johnson, T.D.B., Vol. 19, 1922/766.

Impossible that pasteurisation could be productive of any general impairment of nutrition.—E. Pritchard, L. ii./22, 925.

Thermal Death-point of the Tubercle Bacillus in milk.

As a result of experiments the author draws the following conclusions :

- (1) By using 25 strains of tubercle bacillus no wide difference in the death point was found.
- (2) The thermal death point is practically similar for human and bovine types.

(3) Previous variations in results due to too little care in carrying out experiments.

(4) 20 minutes exposure at 60° C. required to prevent milk so treated carrying infection to the guinea-pig.

(5) 5 minutes at 70° C. required to ensure the same result.

(6) Of the two combinations of time and temperature factors the former excels the latter when the *food value* of the treated milk is also considered.

(7) Until bovine tuberculosis can **be stamped out at its source** pasteurisation is the only safe method of rendering milk safe for human consumption.—F. W. Campbell Brown, L. ii./23,321.

The process may be approximately carried out by plugging convenient sized bottles filled with the quantity for one meal, heating in a pan surrounded with water to nearly boiling point, remove from the fire, cover with a clean cloth and allow to stand for half-an-hour. Then cool rapidly, and store in a cool place.

Milk heated in a closed vessel to 60° C. for 20 minutes becomes sterile as regards micro-organisms.—L. ii./13,1548.

To obviate the **constipating effect** of Pasteurised milk for infant feeding add 5 to 20 grains of *sodium bicarbonate* to the quart of milk, also a little milk sugar. The Sp. Gr. of the final product must be 1.033.

The raising to 190° F. makes milk perfectly safe from contamination with B. tuberculosis, and this does not impair its nutritive value.—N. Raw, B.M.J. i./21,596.

Pasteurisation at 145° F. (62.5° C.) for 30 minutes ensures a non-infective milk so far as T.B. is concerned.—R. G. White, L. i./26,222. Pasteurisation in *closed vessels* at that temperature for 30 minutes, then cooling to under 40° F. renders the milk free from tubercle bacilli and all other pathogenic bacteria.—S. G. Moore, B.M.J. ii./26,855.

See also Nat. Milk Conf., Frequency of bovine infection in the human subject.—B.M.J. ii./22,820.

Danish Pasteurisation means 80° C.—H. A. Cookson, B.M.J. ii./26,963.

Detection of Pasteurisation.

To 5 Cc. of the milk add 1 Cc. of Benzidine Acetate solution 1% and a drop of Acetic Acid; after shaking, 3 Cc. of H₂O₂ are run on to the surface of the mixture.

Unheated milk gives Blue colour.

Heated milk, about 60° C. Faint blue.

„ „ above 70° C. No colour.

We have found this test quite distinctive. Samples of 'Certified Milk' and raw milk respond as stated. 'Household Milk' gives a faint blue.

The number of bacteria reduced by pasteurisation is often only slight as compared with raw milk and a tremendous increase may take place during the cooling process,—Prof. J.M. Beattie, Proc. Nat. Milk Conf. on Pasteurisation Ldn. 1923—quoted by C. Dukes, Bacterology of Food,—1925.

References to the Literature on Pasteurised Milk and Tubercle Infected Milk.

At the National Milk Conference, London, Nov. 6, 1926, it was stated that investigation of a large number of samples of milk in this country showed **6.5% infected with tubercle**. Some 3,000 deaths a year in this country are due to tuberculosis of bovine origin. The remedy agreed on by most speakers was pasteurisation.—L. ii./26,1076.

If the assumptions of speakers at the National Milk Conference are correct, i.e., that Tuberculin-Tested Milk must necessarily be an expensive item, and all milk not from tubercle-free herds must be pasteurised, then the milk supply in our large cities will be reduced to the position of that in New York, where 2% of the supply is Certified Milk sold at 'fancy' prices and 98% is pasteurised. In England it is possible to sell Grade A (T.T.) milk in provincial towns at a price not more than 1d. a quart more than that of ordinary milk, and in London 2d. a quart more. Is it advisable that the people of this country shall admit that pasteurisation is the true remedy or shall we not press forward for the provision of a clean milk free from disease at an economic price—a policy to the best interests of both farmers and consumers?

That there is a **danger of wide-spread pasteurisation** affecting the health of children cannot be denied. The diminished Vitamin supply *can* be made good, but the means or the opportunity to supplement the diet in this way are not always available. The alteration in the relationship of the **diffusible** and non-diffusible **Lime salts** on heating milk is also important from the bone-formation view. 26.4% of the **total calcium** in fresh milk **is diffusible** and in pasteurised milk, *i.e.*, milk heated at 70° C. for 30 minutes it is 20.4% (Note 63° C. is usually considered pasteurisation temperature). A long series of experiments carried out at temperatures ranging between 105—210° F. gave diminution of diffusible Calcium in every case and the coagulation time of the heated milk was prolonged with rise of temperature, until at 205—209° F. no true coagulation took place. Experiments in New York as to the relative efficiency of Certified and pasteurised milk showed that the former alone gave greater increase in body weight in babies than the latter, whether alone or with orange-juice and Cod Liver Oil—the increase with Certified milk was 14%, with pasteurised milk alone 1.7%, plus orange-juice 7.9%, and plus orange-juice and Cod Liver Oil 9.5%. Other experiments showed that pasteurisation causes precipitation of the Calcium, which adheres to the sides of the vessel—with rats fed on pasteurised milk the growth was half normal, while those fed on pasteurised milk plus washings from the vessels showed normal growth. The indiscriminate use of pasteurised by the great majority of the population is not to be recommended.—C. Maddock (Hon. Sec., Grade A (T.T.) Milk Producers Assn.), L. i./27,54.

In reply to a question in the House of Commons on May 25, 1927, Sir Kingsley Wood stated that the **Quantity of pasteurised milk sold** in England and Wales might very provisionally be **put at between 5 and 10% of the total** liquid milk.—L. i./27,1208.

It is estimated that the average daily consumption of fresh milk in Great Britain is probably between 2½ and 2⅙ million gallons and of imported tinned, about 6,500 cwt., equivalent to about 210,000 gallons liquid milk). Certified and Grade A milks constitute about 1% of the fresh milk.—Parl. Notes L.ii./27,208.

The U.S. Public Health Reports (Feb. 11, '27) show that 28 of the milk-borne outbreaks of infectious disease recorded during the last 18 years were attributed to inadequately pasteurised milk—at the same time, it is the belief of the U.S. Public Health Service that pasteurisation of milk 'is the most potent single force operating to **prevent the transmission of milk-borne diseases.**' 'Flash' pasteurisation has disappeared, but there are still many technical difficulties in the way of securing efficient pasteurisation. It is doubtful if the British public is very interested in safe milk yet. There are **only 120 pasteurising establishments** in England and Wales complying with the Min. Health requirements. We cannot expect to get very far with voluntary methods, and ultimately it may be necessary to enforce pasteurisation of all milk except the two upper grades if we really wish to secure a safe milk supply for a public that is not enthusiastic either for or against, but rather expects such matters to be arranged for it by the public health authorities.—Leader, L. ii./27,128.

A cleaner milk supply would bring about a greater demand. Milk ought to be clean and would soon become so if the Profession were to use its influence. There is hardly one of the 230,000 herds in the country which does not contain an infected animal. A certain number of **County Councils have started routine periodical inspections of cattle by Veterinary Surgeons.** The Tuberculosis Order certainly cannot be expected to put things right by itself as the effect of offering compensation to the owners of infected cows is to allow ignorant or unscrupulous farmers to delay notification until the animals have reached the terminal stages of the disease. Even where a case of open infection has been found there is no inducement to the owner to have the rest of his herd examined. Steady progress is being made in the production of **tubercle-free milk**—in 1926 there were 252 herds, comprising **9,100 dairy cows, supplying pure milk.** The greatest disadvantage to the farmer is the absence of a market for this milk. It can be retailed at prices only a little higher than the ordinary and it is certain that a public demand would lower these prices still further.—Leader, L. ii./27,716.

Clean Milk.

It cannot be emphasised too strongly that it is *method* and not equipment which is the all-important factor in the production of clean milk. Owing to practical pioneer work done by the National Institute for Research in Dairying (University of Reading) about one-sixth of the milk supply of Reading is 'Grade A' (T.T.): the retail price in the summer is 3½ per pint and in the winter 4d., as compared with 3d. and 3½d. for ordinary milk. What has been done in Berkshire can be done in other counties. In the U.S.A., by means of what is known as the '**accredited herd**' and '**area eradication plans**', there are **13 million cattle free from tuberculosis** and the districts where they are kept are so hemmed in with regulations and veterinary supervision that it is practically **impossible to reintroduce among them infected cattle**. The Tuberculosis Order throws the onus of diagnosis and reporting suspected cases on the owner, but the owner has not sufficient knowledge to make the diagnosis until the animal is in an advanced stage of disease: the deadly work has been done before the Veterinary Inspector sees the herd. The obvious remedy is periodical inspection of all cattle, and any owner found to have an animal in an advanced stage of tuberculosis which he should have reported should be fined and no compensation paid for slaughter. Only neglectful and indifferent owners would thus be penalised, and it would prevent the present scandal of cows being milked to the bitter end and when no longer of use as milkers reported and compensation claimed. **The inspection of the animal is obviously the job of the Veterinarian, and it is an anomaly that this work is still too often left to the M.O.H. or the Sanitary Inspector.**—Prof. F. T. G. Hobday, — L. ii./27,738.

Dairy Research and the Farmer.

It is often asked whether the work of the National Institute for Research in Dairying has any influence on the production of 'ordinary' milk, sold with no guarantee as to cleanliness. The reply is a decided 'yes.' It is unfortunate that the producer of 'ordinary' milk is paid the same price, whether he endeavours to keep it clean or no, but luckily cleanliness has several advantages from the farmer's point of view—losses from sour milk disappear, udder troubles are reduced, cowmen take a keener interest, and really clean, reliable milk can always find a ready market. The methods in use at the National Institute have been widely adopted by farmers in the district. The clean milk movement has now gathered considerable impetus and the general standard of cleanliness is much higher than a few years ago. The modern farmer's faith in the scientist is much greater than the public realises or he himself admits.—"Dairy Farmer," L. ii./27,740.

According to the **National Milk Publicity Council**, the milk consumption of London has increased from 72 million gallons in 1923 to 117 million gallons in 1927, i.e. 62%. These figures are for rail-borne milk only—it is estimated that a further 5,000,000 gallons per annum are brought into London by road. The increase in the population of Greater London for the same period is less than 1%.—Parl. Notes, L. ii./27,1106.

Infection of children with Bovine Tubercle Bacilli. Unsterilised milk in this country is the vehicle by which tubercle bacilli must most frequently be introduced into the bodies of children. **Cow's Milk containing bovine tubercle bacilli is the cause of 90% of the cases of tuberculous cervical glands in infants** and children residing in Edinburgh and district—in which the research was conducted—and is responsible for by far the larger proportion of tuberculous cervical glands in children during the milk drinking period of life (0 to 5 years). Strong arguments are put forward for protection by legislative measures.—A. Philip Mitchell, B.M.J. i./14,125.

See also numerous refs. re Milk and Childhood under B. Tuberculosis in the Bacteriological Notes Chapter.

Slaughter of Tuberculous Cows.

Mr. Buxton asked the Minister of Agriculture the number of cows affected by tuberculosis which had been slaughtered in 1926 and 1927 in pursuance of the Tuberculosis Order 1925, and whether he was satisfied that the Order was fully operative.—Mr. Guinness replied: **The number of cows**

(including heifers) **slaughtered** under the provisions of the **Tuberculosis Order, 1925**, in respect of **1926 and 1927 is 16,522 and 16,708 respectively**. Local authorities have now completed their arrangements for carrying out the requirements of the Order, and I am satisfied that the Order is properly executed.

Mr. Buxton : Does the Minister not think that in view of the increase, an increase in the staff of inspectors is needed ?

Mr. Guinness : I do not think so : the local authorities seem to be carrying out their duties satisfactorily.—Parl. Notes, L. July 28, 1928.

W. G. Savage (see our Vol. I., p. 934) comments on the 1925 Order as follows: "Owing to lack of coordination between Agricultural Committees and Public Health Committees very little will be accomplished in reducing bovine tuberculosis under the Order. **Whole-time Veterinary Surgeons are necessary for every county of any size.**"

Annual Congress of the Royal Sanitary Institute. The grading of milk '**a magnificent educational gesture.**' The Tuberculosis Order, as at present worked, is of **no value whatever**. A continuing expense with no reduction of tuberculosis and no protection to the public.—W. G. Savage. General admission that the eradication of tubercle was so remote that some method of rendering milk safe must be adopted.—L. ii./28, 229.

The number of **cows which do not react to the tuberculin test** under the clean milk scheme has increased during the past five years by an average of about 1,500 annually, and at the present time these number approximately 12,000. The tuberculin test in the end effects the elimination of all reacting animals from licensed herds. Sir George Newman said : The only way of securing a satisfactory national milk supply is by setting up a high standard and asking producers to raise the standard of their milk accordingly.—'*Daily Telegraph*,' Apl. 17/29.

General References regarding Milk Supply and its Consumption.

Milk consumption and the growth of school-children.

Investigations carried out in an institution near London containing 600 boys showed that an immediate improvement in physique followed the use of fresh cow's milk, recently Pasteurised, as an additional item of food, and this improvement was maintained over a period of from one to three years.—H. C. Corry Mann, Med. Res. Counc. Spec., Rept. Series, No. 105, H.M.S.O., 1926, B.M.J. ii./26,318.

The addition of milk (whether 'separated' or 'whole') to the diet of school-children gave an increase of 20% in height and weight, and improvement in the general condition. **Separated milk** of great value for promoting growth—its nutritive value for children has been under-estimated.—J. B. Orr, Prelim. Rept. on Tests to the Scottish Bd. of Health, L. i./28,203.

Dr. Orr's conclusions were more than justified. The great value of **additional milk** is clearly demonstrated for school-children of all ages, the increase in height in milk-fed groups being actually 1.21%, and in weight 3.75% greater than in the first test, the initial improvement being continued over the second year. The value of separated milk is again shown, there being no significant difference in height and weight (except in the 6-year old group) between the separated milk and the whole milk groups.—G. Leighton and Mabel L. Clark, Second Prelim. Rept. on Tests to the Scottish Bd. of Health, L. i./29,43.

It would be a mistake to conclude from these investigations that separated milk is as good as whole—the home diet was an unknown factor in the experiments. Height and weight are not the only criteria of good health—another important manifestation is the power to resist disease, and subsequent reports would be more valuable if clinical histories were given. At the same time, the fact that the addition of one pint of milk daily produced such striking improvement confirms the contention that large classes of the population suffer as a result of taking too little. Unfortunately, the use of whole milk and butter is expensive, but these results justify their replacement by **separated milk and margarine containing Vitamin 'A'**. A diet of porridge, brown bread, separated milk and Vitamin 'A' margarine would cover almost all nutritive requirements at a minimum of cost. The

distribution of such a diet (at any rate to children, and nursing and expectant mothers) in the distressed areas would prevent under-nutrition and would be not only a measure of properly-regulated charity but one of wise economy.—Leader, L. i./29,29.

The following notes were made of a personal interview with an Official at the Ministry of Agriculture, to whom we are indebted:—

It is the *intention* of the Order that only 'open' cases shall be dealt with.

It would be impossible to deal with all reacting cases. There is no compulsory routine testing of cows, other than for T.T. milk, though many local Public Health authorities undertake this work on their own account.

33-1/3% of the milking cows in the country are **considered reactors** (*i.e.*, approx. 1,000,000 out of an estimated 3,000,000), and if every reactor was slaughtered it would upset the entire milk supply of the country.

The whole problem is not one of money but of practical difficulties.

The only way for a **farmer** to be sure of keeping his herd 'clean' is **to raise it entirely from his own stock**, which of course must be clean in the first place, and to buy in no animals whatever. This means considerable financial hardship to the farmer.

It takes between two and three years to ascertain definitely whether a cow is a reactor or not, *i.e.*, with 6-monthly tests.

One of the difficulties in eradicating the disease is that **pastures become infected from excreta**, etc., and some authorities consider that pastures so infected are not free from infection for at least a year.

Another difficulty is the **smallness and close proximity** of the **farms** in this country, *e.g.*, as compared with those **in the U.S.**, where herds can be **segregated miles from any source of contamination**.

The Americans have been able to make such rapid strides in eradication owing to the fact that only some 2½% of their cows are tuberculous as compared with our 33-1/3%.

All reacting cows do not necessarily give tuberculous milk.

As to cows which are tested for Tuberculin-tested milk and are found to react, no record as to their ultimate use or disposal after eradication from the herd is kept—*nobody knows and nobody cares what happens to them*.

"Sealcone"—a new milk container, made at the Express Dairy Company's Farm at Finchley. It is made of thick paper, sterilised and passed through hot wax. The cone is filled and hermetically sealed. Milk can be kept sweet for a week, and specially cooled milk for a month.—L. ii./29,106.

Veterinary Opinions.

The percentage of tuberculous cows in a herd is not of great importance, as the milk is mixed. **The detection of tuberculous udder infection is not easy** without training in veterinary pathology, hence the farmer can not always be blamed. The Tuberculosis Order, as it stands, can never be more than palliative; its application varies in different counties, many of which have **not yet appointed whole-time Veterinary Officers**.

Infection of other animals may be due to the milk, dung, or material coughed up by the tuberculous cows, and there is considerable room for tightening up of precautions to prevent reinfection of certified herds. **A veterinary health service**, conducted by the united efforts of whole and part-time men on a detailed plan is essential. The plan should include licences for all milk producers who sell milk, but only after inspection of the herd. The inspection must be regular and aided by laboratory observations. If efficient, it will be costly, but the money will be well spent.

Vaccination with B.C.G. Vaccine represents a great advance, but years must pass before judgment on it can be pronounced.—Prof. S. H. Gaiger, Conf. on Animal Diseases, The Veterinary Record, May, 25, '29.

A Veterinary Surgeon's (Mrs. Chas. Lamb) view of the situation is as follows:—

“In my opinion, the present Regulations are totally inadequate for the eradication of tuberculosis in cattle—though such eradication can be the only method of producing milk free from *B. tuberculosis*, both for rich and poor.

“So long as the farmer is left to report cases, it follows that, not only through wilful negligence, but also through ignorance, innumerable cases must go unreported which have probably long been giving tuberculous milk. It is only in the very dangerous cases that an unprofessional eye will detect tuberculosis in cattle, and this stage may have taken two years to develop.

“Next, the **system of inspection at present in force is useless.** In some parts the cows are only clinically examined once a year—in a few counties every six months. But this cannot possibly be adequate. However sharp or hard-working an Inspector may be, he cannot possibly guarantee that a cow he examined clinically nine months ago is not suffering from tuberculosis now. Clinical examination is of no use unless it be conducted, say, every three months, and even then cases would escape which could only be detected by testing. No reacting cows should have a chance of remaining alive and of being passed on to some other unsuspecting owner, as at present happens. **There should be no distinction between ‘open’ cases and other cases,** as at present. All cases are a potential source of danger and should be treated as such. (In 1925 an instruction was sent round that only ‘open’ cases were to be destroyed, and this reduced enormously the number of animals being condemned at that time.)

“Regarding Pasteurising in the big cities, the opinion seems to be one of doubt as to whether this is always carried out efficiently. If it is, it should be effectual in destroying *B. tuberculosis*.

“The grading of milk should be simpler in nomenclature, so that the man in the street can understand what he is buying—and of course all milk should be ‘Tuberculin Tested.’

“It seems to me, however, difficult to lay the blame altogether on the cow for cases in humans. The question seems to depend on whether the bacillus found is of bovine or human type, and unfortunately, the line distinguishing the two seems vague. It is, however, difficult to exonerate the cow in respect of the very numerous cases of abdominal tuberculosis in children under two years of age, unless it were due in some cases to contamination of the milk or food from human sources.

“As to the Tests. Those who use the Intradermal, swear by it (chiefly because it is the least trouble), but I have heard of cases which were not detected by the Intradermal, and which were

detected by the Subcutaneous. So that I should say that until all the methods come to be very thorough, drastic, and reliable ones, the Subcutaneous serves its purpose well enough.

"All the Regulations are a start in the right direction, but it is a pity they are such half-measures. The only way to make anything more effectual come into force is by propaganda."

(The compensation for slaughtering involves obviously a great outlay, hence the 'preference' to compensate for 'open' cases only—*i.e.*, those giving infected discharges of any sort. It may be explained that an animal may have enlarged glands and other typical symptoms, while another may have enlarged and **openly discharging** glands, *i.e.*, abscess formation together with other typical symptoms. The former are *not* to be slaughtered, the latter *are* to be slaughtered—though both are a source of danger to the public and to other cows.)

Milk Preservatives. See also *Food, Preservatives* p. 492.

By the Public Health (Milk and Cream) Regulations 1912, which apply to the whole of England and Wales, **the use of preservatives in milk is prohibited.** "No person shall add, or order or permit any other person to add, any preservative substance to milk intended for sale for human consumption, and that no person shall sell or expose or offer for sale, or have in his possession for the purpose of sale, any milk to which any preservative substance has been added."

Boric Acid in Milk : Detection (1 in 500 will preserve).

This is detected by evaporating and incinerating at least 10 Gm. of the milk and acidifying the ash with dilute hydrochloric acid (using Litmus). A strip of turmeric paper is now placed in the capsule, so as to be only partly wetted by the liquid. Evaporate to dryness at 100° C.

If boron compounds are present, the part immersed in the liquid will turn brownish-red (formation of rosocyanin). On moistening with a drop of caustic soda, green and purple colours will be produced. On re-acidifying with hydrochloric acid, the red colour is restored, and is again changed to green and blue with excess of alkali.

Alternatively make the milk or other substance just alkaline with Barium Hydroxide solution, evaporate and incinerate. Add a few drops of dilute Hydrochloric Acid, a saturated solution of Oxalic Acid and an Alcoholic Curcumin or Turmeric solution, dry on the water-bath and take up with a little Alcohol. Boric Acid, or its salts give intense magenta-red. Reaction is different from, and far more delicate than, ordinary Turmeric Test.—Public Health Lab. Work, Kenwood.

The flame test is well-known. Evaporate to dryness, treat the ash with a few drops of strong sulphuric acid, add a little methyl alcohol, and apply a light. The alcohol will burn with green at the edges of the flame (at the moment of ignition more particularly). We have determined Boric Acid 1 in 5,000 with ease by this method using 10 Cc. of the sample. It will show even 1 in 8,000 but with some uncertainty.

Borax and Boric Acid cannot be differentiated as Borax alone without the use of Sulphuric Acid gave the colour even though the ash of the milk alone was alkaline to Phenolphthalein. If Boron is found titration of the Ash would be the only means of concluding in which form it existed by comparing with an average milk residue Boron free.

Toxic Symptoms.—Gas in the stomach and intestines, colic, pain in the epigastrium and diarrhoea may be caused by excessive consumption of Boric Acid.

Formalin in Milk : Detection.

A teaspoonful will preserve 10 gallons of Milk for 3 days in hot weather.

A large addition can be detected by simply warming ; but it is better to distil the milk : the distillate has the odour of formaldehyde, but the preservative is not wholly volatilised even when evaporated to dryness at 100° C. In employing colour tests for formaldehyde a notably weaker reaction is obtained when milk containing formalin is distilled and the distillate tested than when water containing the same proportion of formalin is similarly treated.

Schiff's Reagent.—Mix 40Cc. of a 0.5% solution of magenta with 250 Cc. of water, add 10 Cc. of sodium bisulphite solution Sp. Gr 1.375, and then 10 Cc. of pure strong sulphuric acid; allow to stand for some time, when it will become colourless. It may also be prepared when required for use by adding sufficient of a solution of sulphurous acid to decolorise some of the magenta solution. If the sulphurous acid is added in large excess, traces of formaldehyde will not be indicated. Reddish violet colour proves presence of formalin. *Other aldehydes, including aromatic aldehydes, also give the reaction.*

It is better to distil as above mentioned or to use Hehner's Test, i.e., purplish violet ring on layering milk on to strong sulphuric acid; but this is also a group reagent for various aldehyde bodies.

The presence of Formalin 1 part in 200,000 can be detected with this Test also by the following modification:—

If to the distillate from a sample of milk one drop of a dilute aqueous solution of Phenol is added and the mixture poured upon some strong Sulphuric Acid in a test tube, a bright crimson ring appears.

Phloroglucin Test.—To 5 or 10 Cc. of the milk add 5 drops of 1% aqueous phloroglucin solution; shake and add 5 drops Liquor Sodæ 30%. Salmon colour (not yellowish tint) indicates addition of formalin. *We found that this test will show 1 of Formaldehyde (actual) in 50,000 of milk.* It is the best and simplest test.

Rimini's Test.—A satisfactory confirmatory test, being almost specific for Formaldehyde. For method of applying see 'Formaldehyde in Urine.' *We found this test will show 1 of Formaldehyde (actual) in 100,000 of milk.*

Formaldehyde added to foods tends to derange metabolism. Wiley in United States investigated the effects of doses of 100-200 millegrams of Formaldehyde (given with milk) on 12 men during 15 days, the total being 2.5 Gm. to each man. Burning in throat, itching rash, retardation of Nitrogen and Sulphur metabolism, acceleration of phosphorus metabolism, and loss in bodyweight were observed. Apart from harmfulness as a milk preservative, its use is inadvisable, as in dilute solution it prevents the growth of acid forming bacteria while not retarding many harmful organisms.

Copper in Milk. Minute amounts of copper added to milk appreciably reduce the anti-scorbutic Vitamin in the course of heating. Where the pasteurising plant is not in good repair or is not well cared for there exists real danger of copper contamination, which may accelerate the destruction of accessory food factors.—B.M.J.i./24,874. See also B.C.A., '28,A.1152.

Test for Stale, Sour or otherwise Bad Milk.

It is known that the addition of Hydrogen Peroxide to fresh, pure clean milk produces slight evolution of Oxygen, while in the case of stale, sour milk, or milk containing pus or blood or from animals suffering from inflamed udders, fevers, etc., the test produces a much larger quantity of Oxygen and that more rapidly.

Our experiments showed as follows:—

(1) With new milk no gas evolution in the first $\frac{1}{2}$ hour. During the next two hours about 0.5 Cc. evolved.

(2) With sour milk (about 2 days sour) gas evolved at once. After 5 minutes 1 Cc. of gas, after 30 minutes 5 Cc. In the next two hours a further 1 Cc.

(The results were obtained using 50 Cc. of milk in a Doremus tube.)

To determine whether a sample has been heated:

Ortho-Metnyl Amino-Phenol Sulphate, or ***Ortol** (which is a mixture of this body with Quinol and is used in photography) has been used for milk testing. One Cc. 1% solution is added to 10 Cc. of milk and followed by 1 drop of ordinary '10 volume' Hydrogen Peroxide. Raw milk, or milk that has not been heated above 75° C, gives a reddish pink colour.

We find this test characteristic—a good colour is obtained.

Heated Milk. The following modifications may also be used to decide whether a sample has been sterilised or boiled. Mix 3 Cc. of milk with 1 Cc. freshly prepared 10% Hydroquinone solution, and about 15 drops of Hydrogen Peroxide. A rose colour appears if the milk has been heated to a high temperature, but otherwise no colour forms, since heat destroys the enzyme responsible for the reaction. The Storch Test consists in adding a drop of Hydrogen Peroxide solution and 2 drops of 2% Paraphenylenediamine solution to 5 Cc. of milk, and shaking. The liquid becomes indigo-violet, unless

the milk has been heated to above 78° C., when the colour remains white.—Public Health Lab. Work, Kenwood. *Neither of these tests are very conclusive. The Hydrokinone must be fresh and unoxidised—recrystallize it if necessary.*

Test for Freshness of Milk (Schmidt-Muller.) The reagent, which should be freshly boiled each day, consists of 5 Cc. saturated Alcoholic solution of Methylene Blue (Zinc Chloride double salt) with 195 Cc. of Distilled Water. One Cc. of the reagent is mixed with 20 Cc. of milk, and the surface is sealed with Paraffin, and the test-tube is then kept at 45—50° C. Fresh milk should remain blue for 12 hours or more, reduction of the Methylene Blue, in the absence of Formalin, being due to bacterial contamination. If the solution is decolorised within 1 hour, the organisms certainly exceed 500,000 per Cc.—Public Health Lab. Work, Kenwood.

A Survey of the Milk Problem.

There is too much 'treatment' of milk and consequently delay prior to its reaching the consumer in the towns. Its flavour is hence spoilt. It may be said that the general run of the poor and a very large proportion of the so-called well-to-do, in our cities, *do not know the flavour of fresh cow's milk.*

The big dairy companies no doubt do their best to supply a milk of good quality, and Pasteurisation as conducted, *e.g.*, by the United Dairies, Ltd., at Scrubbs Lane, Willesden, whose premises we inspected recently, goes a long way towards safeguarding the public health.

That Pasteurising, however, affects the delicate enzymes in milk can be shown by one of the numerous colour tests, using, *e.g.*, Benzidine or Hydrokinone with Hydrogen Peroxide.

Pasteurising also injures the type of soluble Albumin known as Lactalbumin, as confirmed by Dr. Hamill in his Report. It seems to us a pity that this delicate compound cannot be kept intact. A temperature of 65° C. (149° F.) for half an hour reduced a content of 0.395 to 0.333%, while a temperature of 70° C. (158° F.) for half an hour reduced a content of 0.421 to 0.253%.—Stewart. The figures no doubt do not convey the importance of the chemical changes occurring.

A factor of probably great importance is that the percentage of Diffusible Lime is affected adversely by heating. (*See Mattick and Hallett, Jl. Agric. Sci., July, '29, p. 453—462*) :—

The changes in the diffusibility of the Calcium salts into 3% Sodium Chloride solution are very marked. Between 105—120°F. (for $\frac{1}{2}$ hour) the difference was within experimental error: at 135—140°F. the amount of total Calcium becoming indiffusible is about 0.6%, increasing at 145—160°F. to about 2%, and above this to 2.5—3.6%. At all temperatures from 125—209°F. the amount of Calcium diffused from the raw milk was definitely greater than that from the same milk after heating.

It is, however, from the bacteriological aspect that we take exception to Pasteurising. Pasteurising is not a completely safe shield. No stone should be left unturned to stop possible contamination with tubercle bacilli. A large proportion of these organisms, if present, are known to be killed—but the risk remains. Scientific opinion is not agreed as to the thermal death point of the organism.

The measures for preventing the supply of tuberculous milk are contained in the 1915 Act, the Milk and Dairies Order 1926, and the Tuberculosis Order 1925, to which (*antea*) reference may be

made. The onus of taking samples and stopping supplies rests on the M.O.H. The Milk and Dairies Order is subservient to the 1915 Act. The Tuberculosis Order of 1925 is a step in the right direction. The Special Designations Order of 1923 benefits only those who can afford 'Designated' milk.

All this legislation appears to us rather ponderous and complicated. Four or five types of milk are hardly even a commercial proposition. They may be classed as an 'educational gesture.'

We are faced with the fact that of 2,500,000 cows in this country 1,000,000 are tuberculous, and in these circumstances we have difficulty in believing that all *B. tuberculosis* which may get into the milk supply are killed by Pasteurisation. *B. coli*, a far less resistant organism 'gets through' and is searched for officially as a matter of routine.

We were conversing recently with a farmer owning 100 cows. He remarked: 'I suppose it doesn't matter about tuberculosis elsewhere than in the udder?' In point of fact, infection from the lung (coughed up), and faecal contamination are of grave importance.

As to 'Inspection,' we agree with Mrs. Chas. Lamb, as quoted—the system is *useless*.

With regard to the Tuberculin Test, if it is of value we see no reason why all cows should not be tested.

We may add we were discussing the whole subject with Professor G. H. Wooldridge of the Royal Veterinary College recently. His last words were "*No milk is used in my house without being boiled.*"

As a recent statement on the subject, the following should be noted:—

Of 1,605 samples of **London milk examined**, 143, or 8'9%, **contained tubercle bacilli**. Tracing of tuberculous milk to its source made more difficult by introduction of glass-lined **containers holding up to 3,000 gallons**, possibly from over 200 farms—**a single infected milk may infect the whole of the bulk in the tank**. The many opportunities of contamination during transport, in storage, and in distribution, is a factor adverse to the cleanliness of milk of distant origin.—Rept. County M.O.H., 1928, B.M.J., ii./29,272.

Direct Milk Supply—'Thermo-Isolated.'

The existing Milk Trade regime involves first a lengthy water cooling on the farm, then 'churning' in cans or bulk containers by road or rail to the towns, then pasteurising, then cooling again and finally bottling for the consumer.

We suggest as a competitor to warming milk for half an hour at 145° F. (given, of course, 'clean' *tubercle-free* herds, satisfactory sheds and milking) that it should be *refrigerated* on or near the farm and be transmitted virtually direct to the consumer in vessels of suitable capacity—thermo-isolated on the Thermos flask principle. An additional refrigerating plant at the Town Distribution Depot could be added if required. The vessels would be made of a durable type, to withstand rough handling, and would replace the existing bottles. The refrigeration plant, for the sake of economy, would operate for a number of dairy farmers within reasonable distance.

Chemically, the milk would thus be unaltered, and possess all the inherent advantages of uncooked milk. We have determined that refrigeration at 0° C. does not injure the enzymes as Pasteurising does and the 'Cream line' according to our experiments, is **not affected**. Bacteriologically, it can be said that the milk would at least be equal to that of the existing system, and economically the idea would seem a sound proposition.

We made a few observations in the height of the summer temperature (1929) with milk respectively cooled to 0° C. and heated to 100° C. and placed in Thermos flasks and found as follows :

1ST EXPERIMENT. Household Pasteurised.				2ND EXPERIMENT. Non-Pasteurised.			
TIME.	ROOM TEMPER- ATURE.	AFTER COOL- ING TO 0° C.	AFTER HEAT- ING TO 100° C.	TIME.	ROOM TEMPER- ATURE.	AFTER COOL- ING TO 0° C.	AFTER HEAT- ING TO 100° C.
Wed. 10-7-29				Tues. 16-7-29			
12 noon	20° C.	0° C.	80° C.	11 a.m.	25° C.	0° C.	92° C.
2 p.m.	21° C.	0° C.	58° C.	12 noon	26° C.	0° C.	67° C.
4 p.m.	21° C.	0° C.	50° C.	2 p.m.	30° C.	2° C.	49° C.
6 p.m.	21° C.	0° C.	40° C.	4 p.m.	30° C.	4° C.	42° C.
				6 p.m.	29° C.	5° C.	38° C.
Thurs. 11-7-29				Wed. 17-7-29			
9 a.m.	17° C.	5° C.	19° C.	9 a.m.	22° C.	9° C.	23° C.
3 p.m.	20° C.	6° C.	20° C.	11 a.m.	26° C.	10° C.	23° C.
8 p.m.	18° C.	8° C.	20° C.	12 noon	26° C.	10·5° C.	23° C.
				2 p.m.	26° C.	11·5° C.	26° C.
				4 p.m.	29° C.	12·5° C.	27° C.
				6 p.m.	29° C.	13° C.	28° C.

It will be seen that with the room temperature between 20 and 17° C. (68 and 62·6° F.) milk initially at 0° C. rose only 5° C. in 21 hours, and on the subsequent occasion with the prevailing temperature between 30 and 22° C. (86 and 71·6° F.) a corresponding rise from 0° C. to only 9° C. occurred in the same period. It follows that multiplication of bacteria originally present would correspondingly, or in great measure, be prevented.

It is of interest that the milk, whether Pasteurised or Non-Pasteurised, *that we had heated went sour before that which had been cooled.*

(The loss of heat experiments alongside, were conducted merely as a matter of interest.)

By a system worked on these lines, we see no reason why the majority of consumers should not receive milk *within 8 hours of milking*, especially in view of modern road transport facilities. As a matter of additional precaution, if desired, the housewife could kill chance pathogenic organisms by merely scalding her supply.

(Denmark has been sending cooled milk to England in large silicated containers : this is a menace to the home-producer.)

Refrigeration as a modern development of life is in evidence at

every turn. We notice, for example, the air of an Underground Station just opened has to be treated with artificial ice in consequence of the heat from the electric light installation being unbearable.

Hardly a minute of the day goes by without refrigeration of food-stuffs being utilised in some form or other. Milk appears to be the exception. Every other article of food is conserved to-day with the aid of cold-storage. Even our ice-cream blocks are delivered to the door in jacketted vessels by cycle messengers, but the domestic milk is unprovided for.

Given the right kind of thermo-isolated container, *e.g.*, of stainless steel, or some light alloy, we see nothing against the idea. Apparently something allied is embodied in some French patents:

A method of intensive refrigeration from the time of milking to the time of reaching the consumer. The milk keeps well during storage and transport and its properties remain unaltered.—H. Corblin, *Rev. gén. Froid*, 1927, 8, 194. See also *Proc. 5th Int. Cong. Refrigeration*, 1928.

According to Corblin ('*Le Lait*,' Dec. '28, and Jan. '29), frozen milk separates into layers of fat, lactose and casein, which on returning to ordinary temperature do not homogenise. The fats, according to him, are altered, and the milk loses its normal appearance. These troubles are obviated by cooling in a very thin layer (10 mm.) at -15°C . The dairy farmers in the Pyrenees, who supply the Côte d'Azur and the neighbouring towns employ a method of refrigeration based on this process to keep milk fresh during transport. For large scale work refrigerating machinery is needed, and Corblin has taken out patents for same.

The temperature mentioned is far colder than we have in mind. We made some further experiments as follows:—

Raw milk was cooled to 0°C ., as already suggested, placed in Thermos flasks, and after 4 hours, and again after 21 hours, was compared as to flavour and appearance with the fresh milk. There was absolutely no difference in flavour produced by the cold. The '**Critical**' Temperature is below 0°C .

The **Universal non-breakable Vacuum Bottle** is an all-metal vessel on the market, of American make. The quart size costs 42/- and weighs 3 lbs. (We have in mind a vessel costing a fraction of this amount and weighing less.) A quart glass milk bottle as commonly used now weighs 1 lb. 9 oz.

In the ***Electrolux** (T.M. 476,992 : 406,475 : 493,883 : 488,345, Class 6) Apparatus a solution of Ammonia is heated. This releases the Ammonia, which then passes through a condenser and in liquid form enters a vessel (evaporator) containing Hydrogen, where it evaporates, mixes with the Hydrogen and gravitates to another vessel. Here the mixed gas is brought into contact with water from which the Ammonia has previously been driven by heat. The water absorbs the Ammonia and releases the Hydrogen, thus again forming a solution of Ammonia and allowing the Hydrogen to return to the evaporator. (The apparatus was invented by Platen & Munters, and the World rights purchased by A. B. Elektrolux, Sweden.)

The **Frigidaire Cabinet** is worked by evaporating Sulphur Dioxide, and compressing again with a motor. It maintains foodstuffs at $40-45^{\circ}\text{F}$. (or lower for commercial use).

As to the presence of *B. tuberculosis*, we are aware that a section of the Medical Profession virtually ignores tubercle-infected milk as a source of danger, but we are not satisfied with the situation.

We agree that Pasteurising is a helpful procedure, but time will show that as an intermediary safeguard, it cannot be considered the last word in handing milk to the consumer.

Apthous Fever.—(*Foot and Mouth Disease*—see also Vol. I, p. 716.) The milk in this disease presents difficulty to the analyst. The most obvious signs of the infection are ulcers on the mouth, feet, and teats. Unless fever is high, the milk is secreted during the whole course of the disease. It presents different appearances in different cases; in those where there are ulcers on the teat, either externally or just inside, the pus from these ulcers mixes with the milk, and a high fatty residue, from which Cholesterin, Nuclein, Lecithin, and Milk Fat may be separated, results. If, on the other hand, there are no ulcers, and no affection of the udder, the milk in the more severe cases may be deficient in solids, and especially in milk fat, nor does it recover its normal composition until about the seventh or eighth day, when the cow begins to improve. Klein found a micrococcus, either singly, as dumb-bells, or as streptococci—Winter Blyth.

Mammitis, typhus, cholera, typhoid, diarrhoea (*B. Enteritidis Sporogenes*) in relation to milk, are also dealt with by Blyth.

Cream Preservatives.

No person may sell cream which contains any thickening substance. "Thickening substance" means sucrate of lime, gelatin, starch-paste, or any other substance which when added to cream is capable of increasing its viscosity, but does not include cane or beet sugar.—Min. Health Regns. in force since Jan. 1, 1927.

"Thickeners" such as *gelatin*, *starch-paste* and *sucrate of lime* have been used in the past for cream. Mixtures of *Boric Acid* and *Borax* mixed in such proportion so as to be neutral have been used as preservatives. *Saccharin* has been used to mask incipient sourness. *Sodium Salicylate* and *Benzoate* have been used in the hope of their being overlooked after the *Boric Acid* has been detected. *Formalin* and *Sodium Fluoride* are unsuitable. *Hydrogen Peroxide* has also been employed—100 Cc. of 3% to each gallon maintained at 120° F. in a closed vessel for 1½ hours, then 1 or 2 drops of 'Catalase' added to decompose excess of peroxide.

Artificial Cream Act, 1929. (*Came into force June 1, 1929.*)

Prohibits the sale of any substance as cream unless it is that portion of natural milk rich in milk fat which is separated by skimming or otherwise), or artificial cream, in which case the **word cream immediately preceded by the word artificial** must be printed on the container, etc.

Premises must be registered with the Food and Drugs authorities, except when made for domestic purposes, or used on the same premises for making some other article of food, or where it is not supplied except in the unopened receptacles in which it was delivered.

All provisions in previous Acts relating to cream (except as to registration) apply to artificial cream.

'Artificial cream' means an article of food resembling cream and containing no ingredient not derived from milk except water, or any ingredient or material which by virtue of the proviso to Sub-section (2) of Sec. 2 of the Food and Drugs (Adulteration) Act, 1928 (*see p. 491*), may lawfully be contained in an article sold as cream.

The Act does not apply to Northern Ireland.

The first case under the Act came up at Marlborough Street Police Court, on the 13th August 1929, the National Farmers' Union being the prosecuting party, and the charge being the selling of an article described as cream **without the word 'cream' being immediately preceded by the word 'artificial.'** The defence maintained that the prosecution could only be undertaken by the local authority, but the Magistrate ruled otherwise and inflicted a fine of £10 and £7 costs, stating that the labels used by the defendants were misleading.—*Daily Mail*, Aug. 14, 1929.

Reconstituted Cream has been made by emulsifying Butter and Dried Milk. It is a miserable product.

Ice Cream : Bacterial Content.

Of 35 samples of ice cream exposed for sale in London during hot weather the number of colonies grown on Agar in 24 hours at 37° C. ranged from 1 to 1,000 million and over per Cc. It is almost certain there was no 'cream' in them and probably no milk.—W.H.M.

The U.S. Dept. of Agriculture Bureau gives an average bacterial count of 38 millions per Cc. in the summer months.

Eleven samples contained Coliform organisms in 0.000001 Cc., and 17 samples *B. Enteritidis Sporogenes* in a like amount, while streptococci were found in 1 Cc. in 29 samples, 9 being of the long-chained variety.

Whilst no epidemic of food poisoning due to ice cream has been traced to that period, it appears worth while considering whether or not contaminated foods taken in childhood may permanently alter the intestinal flora resulting in later life in puzzling toxæmias and diatheses.—E. G. Rawlinson, L. ii./26, 1267.

Growing tendency for names of articles to lose their meaning. Ice-cream may describe anything. Lemon Cheese may contain no butter, sugar, egg, or lemon. Custard Powder is coloured and flavoured Maize Flour.—B.M.J. ii./25,580.

BACTERIOLOGICAL EXAMINATION OF MILK FOR SUSPECTED SEWAGE OR FÆCAL CONTAMINATION.

Proceed on the lines of a water examination and draw conclusions from the isolation of *B. Coli*. It must be remembered, however, that even the purest milk may show chance contamination of this description. A milk collected with the most stringent precautions in dealing with cows, stables, etc., might possibly show no *B. Coli* at all per Cc. The presence of a considerable number of *B. Coli*, for example 100 per Cc. with the simultaneous presence of *Streptococci* would be grave cause for suspicion of faecal contamination, e.g., in the stables. Again, the presence of *B. Coli* may indicate a diseased udder, for example, mastitis, but the presence of *B. Coli* would in all probability not be caused by the animals drinking *B. Coli* infected water.

The organisms found in milk may be classed as follows:—(i.) Acid producing (100 varieties), the principal member of which is *B. acidilactici*; (ii.) *B. acidibutyrici* (has very resistant spores, not killed by pasteurisation); (iii.) those responsible for fermentation to alcohol, as koumiss, butter milk, red milk, blue milk, &c. (iv.) the mould *Oidium albicans* produces thrush in infants' mouths; (v.) *B. tuberculosis* (a large percentage of cows are tuberculous); (vi.) *Streptococci* associated with contagious mammitis; (vii.) *B. diphtheriae*; (viii.) *B. coli communis* and *B. typhosus*.

Detection of *B. Tuberculosis*—Preferably done by animal inoculation. Failing this the specimen may be stained and searched as directed in the *Bacteriological Notes Chapter*.

With specially conducted milking, etc., the bacterial content only rose above the 10,000 limit on three occasions. The subject of *T. B.* in the faeces of apparently healthy cows discussed.—B.M.J. i./20,365.

The best commercial milk can maintain a standard of less than 10,000 colonies per Cc. for at least 24 hours after milking. It maintains its sweetness at room temperature for average of 6.2 days in winter and 3.3 days in summer.—R. S. Williams, L. ii./21,1386; see also R. T. Hewlett, *ibid* i./22,102.

It is possible for the dirtiest milk (due to bad conditions in barns, dirty cows, etc.) to pass established bacterial standards.—J. Dairy Sci., 1921, 4,430; Y.B.P., 1922,27.

A milk-borne epidemic of septic sore throat in Portland, Oregon. 487 cases and 22 deaths caused by drinking raw milk from one dairy. Similar strains of hæmolytic *Streptococcus* of human type obtained in almost pure culture from the inflamed udder of a cow, from one milker's throat and from the throats of numerous sore throat patients and contacts.—R. L. Benson and H. J. Sears, J.L.A.M.A., per J.L. Trop. Med., Aug. 1/23,257.

See also *B. Tuberculosis postea* and *Graded Milks antea* on the matter in general.

Cellular Elements present in milk are best stained by Jenner's or May-Grunwald's Stain. Sodium Chloride of either 0·7, 0·8 or 0·9% not suitable for washing the cells deposited by centrifuge. Washing with Ox Serum gave better results, causing the least contraction of the cells, of any of the wash liquors tried.—Prof. Hewlett, L. i./15,855.

Normal milk contains polynuclear and polymorphonuclear leucocytes, which may be mistaken for pus cells, as many as 54,300,000 per Cc. have been observed in an apparently normal sample. Mere cell counts do not afford a true criterion of pathological condition of the udder; on the other hand a paucity of cells might also indicate a pathological process.—M.P.C. i./14,457.

All milk contains leucocytes, but do these become converted into pus cells, and how distinguish one from the other? The cell count is increased in milk taken from a cow which is drying off, but the condition is entirely physiological, not pathological. Differential staining should be done by Jenner's method. If an abscess be deep, and has infiltrated the gland, its presence is shown by increased number of phagocytic cells; if acute, the phagocytic activity of the numerous cells is marked; if chronic, and beginning to be shut off by fibrous tissue, the polymorphonuclear cells are less numerous and less sharply defined. The other cells do not appear to be increased in number.—P. C. Varrier-Jones, L. ii./24,537.

"Turning" of milk during thunderstorms accounted for by the usually prevalent high temperature and moisture content of the air favourable to bacterial growth rather than by electrical disturbance.—P.J. ii./12,345.

Condensed Milk is now standardised under Min. Health, *see* Vol. I., p. 588.

The changes in the condition of the milk as a result of condensation are profound and not merely caused by deprivation of water.

In the manufacture of sweetened Condensed Milk, the maximum temperature reached is usually between 80 and 90° C., at which it is kept a few moments. This is not enough to kill many types of bacteria.

Sweetened Condensed Milk is never sterile; sporing aerobic bacilli isolated from 92% of tins and probably present in every sample—decomposition does not necessarily follow. 'Blowing' of tins of sweetened condensed milk almost invariably due to growth and chemical activities of yeasts—no suggestion that these are harmful.

In *unsweetened*, the milk is boiled down under reduced pressure. The sealed tins are heated to 110° or 116° C. for 30 to 40 minutes—the tins are rotated to increase penetration. About 80% of samples found to be sterile, the non-sterile containing chiefly spore-bearing aerobes in small numbers, yeasts being of small significance. Decomposition in condensed milk nearly always due to non-sporing organisms. Longer processing at lower temperature would give results as good as shorter time at higher temperature, without risk of damage to milk.—"Studies in Sweetened and Unsweetened (Evaporated) Condensed Milk," Food Investigation Board of Dept. of Sci. and Indust. Res. W. G. Savage and R. F. Hunwicke, Food Investigation Board, B.M.J. ii./23, 296; L. ii./23,529.

See also Na. 1923,293; C.D., May 24, '24,731.

Lactose Estimation is conducted by the method under Milk.—10 Cc. of a mixture of 1 part milk and 2 parts water by weight are used, or about 3·5 Gm. direct in the flask.

Dried Milk.

The Public Health (Dried Milk) Regulations 1923, which came into force May, 1924, require tins to bear label "Dried Full Cream Milk," "Dried Partly Skimmed Milk," "Dried Machine Skimmed (or Dried Skimmed) Milk," whichever is applicable. Dried full cream milk to contain not less than 26% Milk Fat; dried partly skimmed milk less than 26%, but not less than 8%, and dried machine skimmed less than 8%. Label to state equivalent of parts of milk which receptacle contains. On labels of dried partly skimmed milk statement that contents must not be used for babies except under medical advice, and in dried machine skimmed milk, in large type, "Unfit for Babies." A local authority on finding a consignment of dried milk in district not complying with regulations shall communicate with local authority in district where milk was manufactured or labelled, if in England and Wales, and if elsewhere with Minister of Health.—B.M.J. i./24,124.

Human Milk.

The average composition of human milk is given in Vol. I. (pp. 585 and 588). Note in particular the high proportion of Lactalbumin to Casein (Vol. I., p. 585, and this Vol., p. 467, and the remarkable difference in mineral matter. '*Phosphatide*' in human milk is about half that in cow's milk (cf., p. 467). See also Anal., '28, 78.

In Detroit there is an organisation, with turnover about £2,000 per annum, for the commercial production and distribution of human milk.—L. i./25,450

BUTTER ANALYSIS.**Average Chemical Composition of Unadulterated Butters:**

Water 6.5 to 11.2, Curd 2.4 to 3.1, Salt 1.6 to 2.0, Fat 83.7 to 89.5%

The following data are necessary to determine quality of a specimen.

- (i.) **Estimation of Water:**—Heat 5 Gm. in an air-oven to 110° C. The loss must not exceed 16%, if more suspect careless making or intentional adulteration. **See Food and Drugs (Adulteration) Act. 1928.**
- (ii.) **Estimation of Curd and Salt:**—Melt the residue of (i.) and treat with 10 Cc. ether, filter through tared filter, repeat the process and wash until all ether-soluble matter is removed, dry residue and weigh; the residue consists of curd and salt.
- (iii.) **Estimation of Ash:**—Ignite residue from (ii.) and weigh. Should be wholly salt; confirm this by standard Silver Nitrate solution.
- (iv.) **Estimation of Fat:**—Should be taken by difference by subtracting the sum of percentages of water, curd and salt from 100.
- (v.) **Detection of Foreign Fats:**—Prepare some butter-fat by melting 8 Gm., pour off and filter through dry filter, being careful not to pour any of the water on to same. Saponify on a water-bath 5 Gm. of the clarified fat in a tared flask, capacity about 250 Cc. marked at 150 Cc., with 50 Cc. Alcoholic Solution of Potash (3%) and distil off the alcohol. Dissolve the residual soap in a little hot water, add 25 Cc. Sulphuric Acid (5%) and make up with distilled water to 150 Cc., add a little pumice and capillary glass tubes and distil off 100 Cc., filter same and titrate with N/10 NaOH (using Phenolphthalein). 5 Gm. pure butter-fat should require not less than 25 Cc. of alkali; lard, tallow, beef-fat, &c., require only about 1.5 Cc. coconut fat would require about 7 Cc.

Exception.

In the winter some butters require only about 21 Cc. of alkali, the sample should therefore not be condemned unless it requires less than the minimum amount.

In the light of the recent report on food preservatives, no one can at the moment say what view any particular court would take as to what preservative is at present permissible in butter, other than salt.—C.D., Feb. 14/25,252.

Milk-blended butter is not butter. It is specially defined in Sect. I. of the Butter and Margarine Act, 1907, as "Any mixture produced by mixing or blending butter with milk or cream, other than condensed milk or cream."—C.D., Feb. 14/25,252.

Polenske No. (Zeitsch. Nahr. Genussm. 1904,273). Polenske adopts the Reichert-Wollny process and estimates in the same operation the soluble and insoluble volatile acids. 5 Gm. of the fat are weighed into a 300 Cc. flask and saponified with 2 Cc. Soda solution and 20 Gm. Glycerin by heating.

The flask is cooled below 100° C. and 90 Cc. of hot water and a little powdered pumice are added. When the soap is in solution the fatty acids are liberated with 50 Cc. of H₂SO₄ (50 Gm. in a litre). The flask is then attached to a condenser and distilled so that 110 Cc. of distillate are collected in about 20 minutes. Heating is then stopped. The receiving flask is then removed and a measuring jar is used to collect the drainings of the condenser. The distillate is cooled to 15° C. and shaken and 100 Cc. are filtered off and titrated with N/10 Soda. The number of Cc. (multiplied by 1.1 and corrected to 5 Gm.) is the Reichert-Wollny number.

The remainder of the distillate is poured on the filter paper and then washed with three quantities of 15 Cc. each of water, each of which has been passed

through the condenser, measuring jar, and 110 Cc. flask. These washings are rejected. The 110 Cc. flask is then placed under the filter funnel, and the water insoluble acids are dissolved by passing three quantities 15 Cc. each of Neutral Alcohol through the condenser, measuring jar and filter paper. The alcoholic titrates are titrated with N/10 Soda, using Phenolphthalein as indicator. The number of Cc. required is the insoluble volatile acid number.

In butter fat this number varies with the soluble acids numbers. Polenske (l.c.) gave a range of 1.35 insoluble for 20 soluble, to 3.0 insoluble for 30 soluble. Individual butters may, however, give numbers outside this range. Rideal and Harrison (Analyst 1906, 31, 254) give results of examinations of a number of English butters. Harrison (*ibid.* 1906, 31, 353) showed the variation in insoluble acids number for the same soluble acids number.

Hesse (Chem. Zentr. 1905, 1, 566) says the limits given by Polenske should be higher.—Thorpe, Vol. I., p. 580.

Without this, it is stated, it would be easy to pass a butter as genuine which contained a considerable quantity of *margarine*.

Tuberculous Butter.—Persistence of tubercle bacilli in butter from tuberculous milk. Milk from tuberculous cows was made into butter and guinea-pig inoculations were made from the material. The milks were shown to contain tubercle bacilli and one sample of butter made from naturally ripened milk contained it. The butter made by artificial starting from this milk was similarly infected. The question of persistence of the organism in butter after ice storage, in salted and unsalted, under further investigation.—H. A. Cookson, B.M.J. ii./26,637.

The conclusions of the previous writer arrived at in U.S.A. in 1910. "Tubercle bacilli will retain their vitality and virulence while in butter, under common market conditions, for at least five months."—S. G. Moore, B.M.J. ii./26,855.

MARGARINE.

For recent relative legislation see Food and Drugs (Adulteration) Act, 1928, postea.

Materials used include Beef Fat, Lard, Cotton Seed Oil, Cotton Seed Stearin, Arachis Oil, Olive, Cocoanut, Palm Kernel, Maize and Sunflower Oil. Fats used here are chiefly the vegetable Cocoanut and Palm Kernel Oil. The Reichert-Meissl or Reichert-Wollny numbers give the relative proportion of the lower numbers of the series of fatty acids. Cocoanut and Palm Kernel contain a bigger proportion than most vegetable fats of the esters of these fatty acids. The R.M. number for butter is 25 to 30, and any butter giving a figure below is suspicious.—B.M.J. i./15,855. In support of Margarine; Hygienic Manufacture.—B.M.J. i./15,1032.

Soya Bean, Cocoanut and Cotton Seed Oils probably the principal ones now used. 'Illipe Butter' covers a large variety of solid vegetable fats of totally divers composition, and the term has now lost any special significance. Vegetable substitutes are replacing lard (which is a common constituent), e.g., refined Shea Nut Oil and Shea Nut 'Oleine.' Mutton Fat seldom used owing to flavour.—C.D. ii./27,472.

Maize Oil.

Well refined Maize Oil used as salad oil (usually mixed with edible Cotton and other oils); also used in Margarine manufacture. Non-edible Maize Oil used for making soft soap, and lower qualities for burning oil. Iodine value 115—125; m.pt. of fatty acids 18—20°.—C.D. ii./27,412.

Digitonin has been used in margarine examination, for separating the cholesterol and the phytosterol from Oils and Fats in the form of acetates.

Vegetable oils to the extent of 40 to 90% of the total fat were found in 15 samples—in most cases it was Cocoanut Oil. The food value of all animal and vegetable fat is the same—both yield 9.1 Calories of energy per Gm.—B.M.J. ii./11,959,1336.

The Vitamin Content of Margarine.—*It has been suggested to add Vitamins to Margarine.*

Four brands of margarine bought in the open market—'Viking,' 'Silver Tray,' 'Welcome' and 'Gold Chain'—in which a Vitamin concentrate is

incorporated during manufacture, shown by animal experiments to be equal to the best summer butter in Vitamin A and D content. No sample of butter bought in the open market was found to have a higher Vitamin D content than these margarines. The margarines contained 1.25 antirachitic units per Gm.—K. H. Coward, L. ii./28,727.

FOOD AND DRUGS (ADULTERATION) ACT, 1928.

18 & 19. Geo. 5, Ch. 31.

Part I.—

(1) No person to mix, colour, stain, or powder any article of food with an ingredient injurious to health, or any drug with an ingredient injuriously affecting the quality or potency of the drug, and no person to sell food or drugs so treated.

(2) No person to sell an article of food or a drug not of the nature, substance, or quality demanded by the purchaser, except where an ingredient not injurious to health has been added as a preservative and not to increase the bulk or **conceal inferior quality**, or where the food or drug is the subject of a patent, or is unavoidably mixed with extraneous matter, or where, in the case of whisky, brandy, rum, or gin, it is not adulterated other than by the addition of water and is not reduced to more than 38° U.P.

(4) No person is guilty of an offence if the food or drug is distinctly labelled to the effect that it is mixed with an ingredient non-injurious to health.

Part II.—

(6) It is unlawful to manufacture or sell **margarine** containing more than 10% of fat derived from milk. Every package or parcel containing margarine, margarine-cheese, or milk-blended butter must be clearly marked with the words 'Margarine,' 'Margarine-Cheese,' or 'Milk-blended Butter.'

(8) All **factories** of margarine, margarine-cheese, milk-blended butter or trade butter and all wholesale dealers in these **must be registered** with the Food and Drugs Authority.

(9) Occupiers of such factories and wholesale dealers must keep a register showing the quantity and destination of each consignment, and the register must be open to inspection by Officers of the Ministry of Agriculture and Fisheries.

(10) **If any substance intended for the adulteration of butter** is found in a butter factory the occupier shall be guilty of an offence.

(11) Any person selling or consigning **butter or margarine containing more than 16% water** (whether due to adulteration or not), or milk-blended butter containing more than 24% water shall be guilty of an offence.

(12) **Prohibits the importation** of margarine, or margarine-cheese, adulterated or impoverished milk or cream, condensed, separated, or skimmed milk, any adulterated or impoverished article of food, unless conspicuously labelled as indicated in the Act, also butter and margarine containing more than 16% water and milk-blended butter containing more than 24% water, and any of these latter containing prohibited preservatives or preservatives in excess of the Act.

For the purposes of the Act a food is deemed adulterated or impoverished if it has been mixed with any other substance or if any part has been abstracted so as to affect injuriously its nature, substance, or quality, but it is not deemed adulterated by reason only of addition of preservatives or colouring matter of such a nature and in such quantity as not to render the article injurious to health.

Part III.—

This deals with Administration of the Act. (18) A person purchasing a sample of any article with the intention of submitting it to analysis must notify the seller or his agent of this intention and must then and there divide the sample into three parts, each to be marked and sealed, one to be given to the seller, one retained for future comparison, and one submitted to the analyst.

(25) Every public analyst to report quarterly to the authority appointing him as to the number of articles analysed by him under the Act, the result of each analysis, and the sum paid him in respect of it.

Part IV.—This deals with Legal Proceedings:

Part V.—Miscellaneous. (35) The Act applies also to Scotland and to Northern Ireland subject to small modifications.

Came into operation 1st January, 1929. The Fourth Schedule to the Act repeals the Sale of Food and Drugs Acts 1875–1899 and 1927 with certain exceptions, as follows:—

ENACTMENTS REPEALED.

(Except (Sect. 37) as regards Analyses, Orders, etc., under the old Acts.)

Session and Chapter.	Short Title.	Extent of Repeal.
38 & 39 Vict. c. 63	The Sale of Food and Drugs Act, 1875	The whole Act, except secs. 30, 31 & 36.*
42 & 43 Vict. c. 30	The Sale of Food and Drugs Act Amend. Act, 1879	The whole Act.
50 & 51 Vict. c. 29	The Margarine Act, 1887 –	The whole Act.
55 & 56 Vict. c. 55	The Burgh Police (Scotland) Act, 1892	In sec. 432 the words “under the Sale of Food and Drugs Act, 1875, and also.”
62 & 63 Vict. c. 51	The Sale of Food and Drugs Act, 1899	The whole Act.
7 Edw. 7. c. 21 –	Butter and Marg. Act, 1907	The whole Act.
4 & 5 Geo. 5. c. 46	The Milk and Dairies (Scotland) Act, 1914	Section twenty-seven.
5 & 6 Geo. 5. c. 66	The Milk and Dairies (Consolidation) Act, 1915	Section nine and the Third Schedule.
11 & 12 Geo. 5. c. 32	The Finance Act, 1921 –	Section twenty-three.
11 & 12 Geo. 5. c. 42	The Licensing Act, 1921 –	Section ten.
17 & 18 Geo. 5. c. 5	Sale Food Drugs Act, '27 –	The whole Act.

*These Sections refer to the inspection, analysis and destruction of *Tea*.

FOOD PRESERVATIVES.

The Minister of Health issued Regulations based on recommendations of the Departmental Committee on the Use of Preservatives and Colouring Matter in Food and providing for the prohibition of the importation and sale of articles of food to which preservatives and other specified substances have been added. These Regulations in general came into operation on January 1, 1927.

The Regulations prohibit the use in foodstuff and drinks, of preservatives except those mentioned below, and then on condition that they do not contain a larger proportion than is specified, and are properly labelled.

“Preservative” includes any substance which is capable of inhibiting, retarding or arresting the process of fermentation, acidification or other decomposition of food or of masking any of the evidences of putrefaction.

The term does not include Salt, Saltpetre, Sugars, Vinegar, Acetic or Lactic Acid, Alcohol, or potable Spirits, Spices, Herbs, Hop Extract, Essential Oils used for flavouring, Glycerin or any substance added by process of curing known as smoking.

PERMITTED PRESERVATIVES.

Food.	Preservative.	Parts per million.
(1). Sausage and sausage meat containing raw meat, cereals and condiments	SO ₂	450 = 3.15 grains per lb.
(2). Fruit and fruit pulp not dried:—		
(a) Cherries	SO ₂	3,000 = 21 “ “ “
(b) Strawberries and Raspberries	SO ₂	2,000 = 14 “ “ “
c) Other fruit	SO ₂	1,500 = 10.5 “ “ “

PERMITTED PRESERVATIVES—*continued.*

Food.	Preserva- tive	Parts per million.
(3) Dried Fruit :—		
(a) Apricots, peaches, nectarines, apples and pears	SO ₂	2,000 = 14·0 grains per lb.
(b) Raisins and sultanas	SO ₂	750 = 5·25 „ „ „
(4) Unfermented grape juice and non- alcoholic wine made from such grape juice if labelled in accord- ance with the rules contained in the second schedule to these Regulations	Ac. Benz.	2,000 = 140·0 grains per gall.
(5) Other non-alcoholic wines, cordials and fruit juices, sweetened or un- sweetened	SO ₂ or Ac. Benz.	350 = 24·5 „ „ „ 600 = 42·0 „ „ „
(6) Jam (including marmalade and fruit jelly prepared in the way in which jam is prepared)	SO ₂	40 = 0·28 grains per lb.
(7) Crystallised glacé or cured fruit, including candied peel	SO ₂	100 = 0·7 „ „ „
(7a) Fruit and fruit pulp not otherwise specified in this schedule ..	SO ₂	350 = 2·45 „ „ „
(8) Sugar (including solid glucose) and cane syrups	SO ₂	70 = 0·49 „ „ „
(8a) Cornflour (maize starch) and other prepared starches	SO ₂	100 = 0·7 „ „ „
(9) Corn Syrup (liquid glucose) ..	SO ₂	450 = 3·15 „ „ „
(10) Gelatin	SO ₂	1,000 = 7·0 „ „ „
(11) Beer	SO ₂	70 = 4·9 grains per gall.
(12) Cider	SO ₂	200 = 14·0 „ „ „
(13) Alcoholic wines	SO ₂	450 = 31·5 „ „ „
(14) Sweetened mineral waters ..	SO ₂ or Ac. Benz.	70 = 4·9 „ „ „ 120 = 8·4 „ „ „
(15) Brewed Ginger Beer	Ac. Benz.	120 = 8·4 „ „ „
(16) Coffee Extract	Ac. Benz.	450 = 31·5 „ „ „
(17) Pickles and Sauces, made from fruit or vegetables	Ac. Benz.	250 = 1·75 grains per lb.

Sulphur dioxide includes sulphites, and benzoic acid includes benzoates, calculated respectively in terms of sulphur dioxide and benzoic acid.

LABELLING.—Special labelling applies to *Sausages, Sausage Meat, Coffee Extract, Pickles and Sauces* and (where proportion of Benzoic Acid exceeds 600 parts per million) *Grape Juice and Wine*. These must bear a label stating the contents are preserved, *e.g.*, “These Sausages contain Preservative,” and in the case of grape juice and wine where it applies “and is not intended for use as a beverage.”

The retailer must exhibit a notice in a conspicuous place to the effect that the goods in question contain preservative.

Departmental Committee's Report.

Preservatives may be used to mask unsoundness, or careless methods of production, storage and distribution. A dose of **Boric Acid**, the most commonly used preservative, is **not completely excreted** from the system **for five days**, and the tissues are never free—the Committee considered its prohibition justified. **Sodium Sulphite**, in amounts employed in foods, has no specific toxic action, but is not harmless, as Sulphur Dioxide liberated may cause dyspeptic symptoms. The putrefactive odour of decaying meat is removed by treatment with Sodium Sulphite, and the red, fresh appearance restored. Prof. A. J. Clark, representing the B.M.A., considered that **Formaldehyde** and **Fluorides** should be prohibited, as they are definitely toxic, as also **Borax** preparations on account of cumulative action, and **Salicylic Acid** and **Salicylates** on account of powerful physiological action. Preservatives are used in a haphazard way, or even in ignorance, and often no effort is made to do without them. The Committee saw no reason why the sale of

cream should not be conducted on the same lines as milk, *i.e.* without preservatives. They recommended that after two years of grace preservatives in butter and margarine should be prohibited. Addition of preservatives to sausages undesirable, and should be regarded as a concession to trade necessities, which should eventually be dispensed with. Use of preservatives for packing and dusting of hams unnecessary. Recommendation that use of preservatives in liquid eggs should be prohibited—freezing an alternative. Preservatives should be unnecessary in alcoholic wines of ordinary strength, but where impracticable Sulphur Dioxide is permitted in amounts not exceeding 3 grains per pint. The Committee finally recommended that preservatives be prohibited in all articles of food or drink, offered or exposed for sale, whether manufactured in this country or imported, except with certain exceptions which are given *antea*.

The method of estimating preservatives to be prescribed by the Ministry of Health. Sale of food preservatives should be illegal unless bearing descriptions indicating composition and strength, and are free from impurities, containing not more than 1/100 gr. Arsenic or 1/7 gr. Lead per lb.—B.M.J. ii./24, 290,828,829. See also B.M.J. ii./25,349; i./27,70.

See also *Milk Preservatives*, p. 480 and in addition, *Public Health (Preservatives in Food) Amendment Regns.* 1926 and 1927, and for earlier information on the matter *E.P. XVIIIth Edn.*, Vol. II., pp. 482,483.

Earlier Refs.

Formaldehyde irritates the mucous membrane, and prolonged use may cause inflammation of the liver and kidneys. It combines with the proteins of food, rendering them less digestible, and its excretion is slow. The use of Formaldehyde should be banned in all cases. INTERIM REPORT OF FOOD PRESERVATIVE COMMITTEE, 1924.—Na. 114, '24,448.

It has been suggested that chemical preservatives may be prejudicial by exerting a selective action on bacteria, restraining the putrefactive types, so that the food appears sound, while allowing more pathogenic bacteria to develop.

A fact of general applicability is that the preservatives are mostly substances foreign to the animal body and are **excreted by the kidneys**. This organ is particularly sensitive to chemical substances so secreted, and it is therefore a reasonable supposition that their elimination may be locally harmful, particularly to those with defective or damaged kidneys.—Food Poisoning, Savage.

Being inimical to the life of putrefactive organisms, preservatives **must exercise a retarding effect upon the activity of the enzymes** concerned in ordinary digestion, and they facilitate an uncleanly, slovenly treatment of food, rendering it possible to preserve articles in incipient decomposition for some time with an appearance of freshness.

Salicylic Acid is depressing, liable to be cumulative in action, and has irritant effect on the kidneys. Benzoic Acid is irritating; Formalin delays gastric digestion, and Sulphurous Acid is a gastric irritant.

The presence of preservatives in **canned articles** which have been sterilised by heat, indicates that the addition was made, prior to canning, to **check decomposition**. With good materials, **their use is unnecessary**.—Public Health Lab. Work, Kenwood.

Liquid egg containing Boric Acid is refused entry into the U.S.A. for use as a food. In a London suburb a sample of sponge cake was found to contain 35 grains of Boric Acid per lb., the source of which was egg yolk shipped from China.—per P.J. i./23,487.

Dried Eggs.

Total number of viable bacteria varies, but in general is greater in that dried on vacuum drum than that prepared by the spray process, results varying from 350 to a million per Gm. of liquid egg in the former case, and from 45,000 to over 2 millions in the latter case. The characteristic smell of doubtful eggs is almost lost in the drying process.—per Analyst, '26,98.

Preservatives of meat extract and vegetable infusions (Senna Leaf). SO₂, 0.3% and several others was found ineffectual. Sodium Benzoate (0.25%) preserved in acid solution but fermentation occurred in alkaline and neutral media. Glycerin 45% could not be relied on in acid or neutral media but was effective in alkaline solution. Benzoic Acid, Salicylic Acid, Glycerin and

Alcohol were found to be the best; Benzoic better than Salicylic Acid. Formaldehyde 0.05% preserved in all solutions. It approaches the ideal.—C.D., June 24/22,813.

In America "canning compounds" are sold, and an example is given of one consisting of Boric Acid 95% and Sodium Chloride 5%. This had a selective antiseptic action, inhibiting the growth of some varieties of *colon bacilli*, but *B. enteritidis*, *B. paratyphosus* and *B. typhosus* and others grew readily in the concentration of the compound, which would be used in canning.—J.A.M.A., April 14/23, per P.J. i./23,431.

A suggestion to retain Boric Acid as a preservative for meat products, since, unlike Sulphur Dioxide, it does not remove the taint from unwholesome food. Its deleterious effects are probably greatly exaggerated, since workers in the Saffrines of Tuscany may excrete 8 grains daily, and yet the death rate is less than that of Italy in general.—C.D. i./25,196.

Ptomaine poisoning in man is exceedingly rare; the majority of the cases of food poisoning are due to living specific microbes implanted in food or drink, and small quantities of Boric Acid would neither prevent their access nor kill them if present. Food, such as sausages, containing preservatives, has often been associated with acute gastro-enteritis. Boric Acid would keep food 'free from taint,' but it might mask a far greater danger than mere taint. Greater care needed in the handling of food and the prohibition of preservatives enforces this. It is **monstrous to insinuate that the Ministry of Health has done wrong in putting a stop to the doctoring of food** by chemicals.—A. Rutherford, L. ii./28,768.

Aniline Dyes used in Colouring Foods.

The following aniline dyes have been found by various authorities to be **harmless for colouring foods**. Many were given in a list issued by the National Confectioners' Association of the United States in 1899, and to these have been added other colours, specially indicated, which are permitted by the Governments of Australia, Canada and the United States. The number placed before each colour is that of the COLOUR INDEX OF THE SOCIETY OF DYERS AND COLOURISTS (1924), which is intended to be the standard reference book of the English-speaking countries.

*The dyes marked with a * are stated in the Colour Index to be actually used for colouring edibles.*

The use of none of these dyes is prohibited by the Public Health (Preservatives, etc., in Food) Regulations, 1926-27. These Regulations render the use of the **following colouring matters illegal**:

1.—Compounds of Antimony, Arsenic, Cadmium, Chromium, Copper, Mercury, Lead and Zinc.

2.—Gamboge.

3.—Picric Acid (7), *Syn.* Carbazotic Acid; Victoria Yellow (8), *Syn.* Saffron Substitute and Dinitro Cresol; Manchester Yellow (9), *Syn.* Naphthol Yellow and Martius Yellow; Aurantia (12), *Syn.* Imperial Yellow; Aurine (724), *Syn.* Rosolic Acid and Yellow Coralline.

The Canadian regulations forbid the use of aniline dyes containing more than 10 parts per million of Arsenic, As_2O_3 , or heavy metals (Iron excepted), and the dyes must not be used in quantities exceeding two grains per lb. (1 in 3,500). The adoption of any colour for pharmaceutical or toilet preparations is governed by the composition of the article, alkalies or acids affecting some of the dyes, whilst the fluorescence of colours, such as Eosine, may be objectionable in a medicine but suitable in a toilet preparation.—C.D. '24,438.

Blue.

- 689 **Gentian Blue 6B**, *Syn.* SPIRIT BLUE, ANILINE BLUE.

The hydrochloride, sulphate or acetate of phenylated *p*-Rosaniline and Rosaniline. Insoluble in water. The acetate is readily soluble in Alcohol, the sulphate and hydrochloride sparingly.

- 861 **Coupler's Blue**, *Syn.* WATER-SOLUBLE INDULINE.

Mixtures of Amino-diphenyl-diamino-triphenyl-triamino and Tetraphenyl-tetramino-phenyl-diphenazonium-chloride and sulphonate. Soluble in Alcohol and Water.

- 1180 **Indigo Carmine** (Aus., Can., U.S.A.).

Sodium salt of Indigotin-5 : 5'-disulphonic acid.

Soluble in Water, sparingly in Alcohol.

Green.

- 670* **Light Green S.F. Yellowish** (Aus., Can., U.S.A.).

Sodium salt of Dibenzyl-diethyl-diamino-triphenylcarbinol tri-sulphonic acid anhydride.

Soluble in Water, almost insoluble in Alcohol.

Picric Acid gives no precipitate (distinction from green basic dyes).

Brown.

- 331* **Bismark Brown G** (Aus.).

Hydrochloride of Benzene-*m*-diazo-bis-*m*-phenylenediamine.

Soluble in Water and Alcohol.

- 480 **Chrysamine R**.

Sodium salt of Ditolyl-diazo-bis-salicylic acid. Water—Soluble.

Orange.

- 26 **Crocein Orange**.

Sodium salt of Benzene-azo- β -naphthol-6-sulphonic acid.

Slightly soluble in Water, moderately in Alcohol.

- 150* **Tropaeoline 000** No. 1, or Orange 1 (Aus., Can., U.S.A.).

Sodium salt of *p*-sulphobenzene-azo- α -naphthol.

Soluble in Water and Alcohol.

Red.

- 46 **Archil Substitute**.

p-Nitrobenzene-azo- α -naphthylamine-4-sulphonic acid

Aqueous solution reddish-brown.

- 79* **Ponceau 2R**, *Syn.* SCARLET R.

Sodium salt of *m*-Xylene-azo- β -naphthol-3 : 6-disulphonic acid

Yellowish-red solution in Water, insoluble in Alcohol.

- 80* **Ponceau 3R and 4R**, *Syn.* CUMIDINE RED (Aus., Can., U.S.A.).

Sodium salt of Cumene-azo- β -naphthol-3 : 6-disulphonic acid.

Ponceau 3R is made from crude Cumidine, and Ponceau 4R from Pseudo-Cumidine.

Water—cherry-red solution ; slightly soluble in Alcohol.

- 88* **Acid Bordeaux**.

Sodium salt of α -Naphthalene-azo- β -naphthol-3 : 6-disulphonic acid.

Soluble in Water, moderately soluble in Alcohol.

- 179 **Carmoisine**, *Syn.* AZORUBINE.

Sodium salt of 4-sulpho- α -naphthalene-azo- α -naphthol-4-sulphonic acid. Soluble in Water.

- 182 **Fast Red E**.

Sodium salt of 4-sulpho- α -naphthalene-azo- β -naphthol-6-sulphonic acid. Soluble in Water and moderately in Alcohol.

- 184* **Amaranth** (Aus., Can., U.S.A.).

Sodium salt of 4-sulpho- α -naphthalene-azo- β -naphthol-3 : 6-disulphonic acid. Soluble in Water, sparingly in Alcohol.

- 370 **Congo Red**.

Sodium salt of Diphenyl-diazo-bis- α -naphthylamine-4-sulphonic acid. Soluble in Water.

- 677* **Magenta**, *Syn.* FUCHSINE, ROSEINE (Aus.).

Mixtures of *p*-Rosaniline and Rosaniline Hydrochlorides.

Soluble in hot Water, and in Alcohol. Soluble in Amyl Alcohol (useful for detection in wine).

- 692 **Acid Magenta**, *Syn.* ACID FUCHSINE.

Mixture of salts of di- and tri-sulphonic acids of *p*-Rosaniline and Rosaniline. Soluble in Water, almost insoluble in Alcohol.

768 Eosine.

Sodium or Potassium salt of Tetrabromofluorescein.
Soluble in water and Alcohol.

773* Erythrosine (Aus., Can., U.S.A.).

Sodium or Potassium salt of Tetraiodofluorescein.

774 Phloxin.

Potassium salt of Tetrabromo-di-chlorofluorescein.
Aqueous solution fluorescent.

777 Rose Bengale.

Potassium or Sodium salt of Tetra-iodo-dichlorofluorescein.
Aqueous solution not fluorescent.

Violet.**279 Wool Black.**

Sodium salt of *p*-sulpho-benzene-azo-*o*-sulphobenzene-azo-*p*-tolyl- β -naphthylamine. Soluble in Water.

315 Naphthol Black B.

Sodium salt of 6 : 8-disulpho- β -naphthalene-azo- α -naphthalene-azo- β -naphthol 3 : 6-disulphonic acid. Soluble in Water.

463 Azoblue.

Sodium salt of Ditolyl-diazo-bis- α -naphthol-4-sulphonic acid.
Soluble in Water.

680 Methyl Violet.

Mixtures of hydrochlorides of higher methylated *p*-Rosanilines.
Soluble in Water and Alcohol.

846 Mauveine.

Mainly Amino-phenylamino-*p*-tolyl-ditolazonium sulphate
Insoluble in cold Water, soluble in Alcohol.

Yellow.

(Water soluble).

10* Naphthol Yellow S. (Aus., Can., U.S.A.).

Potassium or Na. salt of 2 : 4-dinitro- α -naphthol-7-sulphonic acid.

16* Acid Yellow.

Sodium salt of Aminoazo benzene-di (and mono-) sulphonic acid.

The aqueous solution has a neutral action, mineral acids change the colour to a bright red, yellow being restored by the addition of alkali. Used for colouring milk (1 in 200,000), Egg Powders—Custard prepared for table contains about 1 in 40,000..

364 Brilliant Yellow, Syn. PAPER YELLOW.

Sodium salt of 2 : 2¹-disulphostilbene-4 : 4¹-diazo-bis-phenol.

640* Tartrazine (Can., U.S.A.).

Sodium salt of 4-*p*-sulphobenzene-azo-1-*p*-sulphophenyl-5-hydroxy pyrazol-3-carboxylic acid.

A yellow powder almost unaffected in colour by acids or alkalis. When Tartrazine is reduced Sulphanilic Acid is formed. Used for Lemonade, etc., a common proportion being 1 in 500,000.

Yellow (Oil soluble).**15* Aminoazobenzene.**

Aminoazobenzene Hydrochloride (for fats and cheese).

17* Amidoazotoluol.

Aminoazotoluene or HCl salt (for fats, wax and margarine).

19* Oil Yellow.

Dimethylaminoazobenzene or Benzene-azo-dimethyl-aniline (for oils).

22* Oil Yellow A.B. (U.S.A.).

Benzene-azo- β -naphthylamine (for oils and fats).

61* Oil Yellow O.B. (U.S.A.).

o-toluene-azo- β -naphthylamine (for oils and fats).

Other harmless colouring agents are Madder, Logwood, Annatto, Turmeric, Marigold, Chrysophanic Acid and Saffron. Naphthol Green, Metanil Yellow, Bismark Brown, Methylene Blue are stated to be more or less poisonous. Certain dyes, Rosaniline for example, are liable to contain Arsenic, such as by the use of Arsenic Acid as oxidising agent, or from the use of crude Oil of Vitriol containing Arsenic.—Kenwood, Public Health Laboratory Work.
Of the synthetic aniline dyes relatively few are considered harmless in other countries.—Final Report of the Food Preservative Committee, 1924 v. antea.

Annatto Substitute.

Is a mixture of Acid Brown No. 1 (10 parts) and Acid Yellow (8 parts). *Acid Brown* is the Sodium Salt of Para-Sulpho-Benzene-Azo-Metatoluylene-Diamine (4) ($\text{SO}_3\text{Na})\text{C}_6\text{H}_4\text{N}:\text{NC}_6\text{H}_2(\text{CH}_3)(\text{NH}_2)_2(1.5.2.4.)$.

A dark brown powder with occasional yellow specks dissolving easily in water. The solution has a neutral reaction and is of a dark red colour, becoming yellow when greatly diluted. Mineral Acids change the solution to a bright red. Alkalies return original colour.

Used for the same purposes as the vegetable colour (has approximately 25 times the tinctorial power of the commercial extracts of the fruit, of which 1 tablespoonful is added to 30 lbs. cheese, i.e., 1 part in 960) for tinting Milk, Butter, Cheese, (1 in 24,000), haddocks, etc.

Bixæ Folia, Ph. Ned. IV. (*Bixaceæ*). The leaves of *B. Orellana*. Annatto is obtained from the seed.

Annatto Extract.—Bixin related to *m*-xylene is the essential colouring matter. The Extract is usually strongly alkaline.

In the amount used Egg Yellow, Lemon Yellow, and Annatto Substitute are thought to be harmless.—S. Rideal.

ANNATTO.—A sample (rejected) gave 72.0% matter insoluble in boiling alcohol and contained 18.15% moisture. Another gave 8.5% insoluble.—Evans.

Chrysoidine has been used, but there is not sufficient evidence of toxicity to justify prohibition of such colouring matters.—Mr. Neville Chamberlain.

Chrysaniline, a poisonous dyestuff, used by hawkers in some parts of the country, to colour unripe oranges.—P.J. i./25,618.

Permitted colours in U.S.A. Ponceau 3R, Amaranth, Erythrosine, Orange I, Naphthol-Yellow S, Tartrazine, Yellow AB, Yellow OB, Guinea Green B, Light Green SF yellowish, Indigotin.—Y.B.P., '26,82.

MOULD INHIBITION BY MEANS OF VARIOUS PRESERVATIVE SUBSTANCES.

We have conducted experiments to determine the minimum strength of Benzoic, Boric, Salicylic and Sulphurous Acids, in aqueous solution, which would successfully inhibit the growth of the under-mentioned moulds. Sodium Benzoate and Saturated Solution of Clove Oil were also included in the investigation.

Aspergillus Glaucus.

Penicillium Expansum.

Penicillium Glaucum.

Rhizopus Nigricans.

Thamnidium Elegans.

METHOD.—

10 Cc. of the solutions tested were inoculated with 48 hour growths of the various moulds. The tubes were gently agitated, to ensure even distribution of the spores, and after 10 minutes 0.1 Cc. was transferred to tubes of Czapeck's Medium.

In some instances, notably *Penicillium Glaucum*, an abundant growth in 24 hours was observed, but in the results given on the next page 48 hours were allowed.

For inoculation pure cultures were used of the moulds (48 hours old) on Czapeck's Medium, as maximum active spore formation takes place during that period.

(Czapeck's Medium, Brooks' Modification, by courtesy of the National Collection of Type Cultures, is: Magnesium Sulphate 0.5, Potassium Dihydrogen Phosphate 1, Potassium Chloride 0.5, Ferrous Sulphate 0.01, Sodium Nitrate 2, Cane Sugar 15, Agar 20, Water 1,000. Autoclave lightly 10 minutes at 110° C.)

Control experiments were carried out in each instance and the whole series was cultivated in daylight at a temperature of 20-25° C. The results were as follows:—

PRESERVA- TIVE.	MOULD.	STRENGTHS IN PARTS PER MILLION.					REMARKS.
		200	500	1000	2000	3000	
Benzoic Acid	<i>Aspergillus Glaucus</i> ..	+	—	—	—		Sodium Ben- zoate 3,000 ppm. does not inhibit growth of these moulds.
	<i>Penicillium Expansum</i>	+	+	+	+		
	<i>Penicillium Glaucum</i>	+	+	+	+		
	<i>Rhizopus Nigricans</i> .	+	+	+	+		
	<i>Thamnidium Elegans</i>	+	+	+	+		
Boric Acid.	<i>Aspergillus Glaucus</i> ..	+	+	+	+		Abundant re- production after 24 hrs. 20,000 ppm. does not inhibit any of the moulds.
	<i>Penicillium Expansum</i>	+	+	+	+		
	<i>Penicillium Glaucum</i>	+	+	+	+		
	<i>Rhizopus Nigricans</i> .	+	+	+	+		
	<i>Thamnidium Elegans</i>	+	+	+	+		
Clove Oil (Satd. aq. soln.)	<i>Aspergillus Glaucus</i> .						Does not inhibit growth of moulds tested.
	<i>Penicillium Expansum</i>						
	<i>Penicillium Glaucum</i>						
	<i>Rhizopus Nigricans</i> .						
	<i>Thamnidium Elegans</i>						
Salicylic Acid	<i>Aspergillus Glaucus</i> .	—	—	—	—		+ after 96 hrs. in 200 ppm. Slight growth in 500 ppm. in 36 hrs. Abundant growth in 200 ppm. in 36 hrs.
	<i>Penicillium Expansum</i>	+	—	—	—		
	<i>Penicillium Glaucum</i>	+	+	—	—		
	<i>Rhizopus Nigricans</i> .	+	—	—	—		
	<i>Thamnidium Elegans</i>	+	—	—	—		
Sulphurous Acid	<i>Aspergillus Glaucus</i> .	+	—	—		—	Growth in 200 & 500 ppm. after 36 hrs.
	<i>Penicillium Expansum</i>	+	—	—		—	
	<i>Penicillium Glaucum</i>	+	+	—		—	
	<i>Rhizopus Nigricans</i> .	+	+	—		—	
	<i>Thamnidium Elegans</i>	+	—	—		—	

Sulphurous Acid was found the most effective, 1,000 parts per million (or 0.1%) being sufficient to prevent growth under ideal conditions (medium, temperature, etc.). Although the acid in this proportion successfully prevents mould growth, its use as a food preservative is limited, as the amount permissible in most cases is in the neighbourhood of 100 to 200 parts per million. *v. p.* 492, 493.

Nipagin 'M.' *Syn.* METHYL-*p*-HYDROBENZOATE (*cf.* Vol. I., p. 9) is used for syrups (while hot) in proportion of 0.025 to 0.075%. It is soluble in *hot* solutions and in Alcohol. An Alcoholic solution may be added to the aqueous.

Fruit Pulps.—The only preservative in use is SO₂, either as such, or rarely as Calcium Acid Sulphite. Employed in the proportion of 1 part of the 5% solution to 40 of pulp. This is very effective.

Jams.—SO₂ in the pulp is dispersed by the boiling process. The resulting jam is either free or contains minute amounts, *e.g.*, 10 parts per million (40 is the maximum permitted).

To ensure freedom from mould growth, the jam must contain at least 66% of total sugars.

Sauces and Pickles.—The Vinegar inhibits moulds and yeasts. The acidity calculated as Acetic Acid should not be below 3%. Where this acidity is objectionable the product is 'sterilised' by heating at 180° F.

Thymol, Carvacrol, and the volatile oils of Mustard, Cinnamon and Clove possess marked fungicidal powers and hence are suggested in treating mycotic infection.—*Jl. A.M.A.*, ii./27, 1836.

GAS POISONING.

Phosgene, Chlorine, Dichlorethylsulphide, and the tear gas Xylyl Bromide—effects—*Sir W. P. Herringham, L. i./20, 423, 437.* (See also Vol. I., p. 1101.)

Dichlorethyl-Sulphide. Absorbent powders such as Cocoa-nut Charcoal, Fullers Earth, Talc, etc., found efficacious.—*T. Sollman, Jl. Pharm. & Exp. Therap.*, January, 1919.

Dichlor-ethyl Sulphone is of the same order of activity as Dichlor-ethyl Sulphide, while Dichlor-ethyl Sulfoxide is practically inert.—*E. K. Marshall Jr., and J. W. Williams, Jl. Pharma. and Exp. Therap.*, Nov., 1920.

Ethoxydichloroarsine and allied bodies, observations on (for war purposes).—*A. McKenzie and J. K. Wood, J.C.S. Apl.* 1920, 406.

Diphenylchlorarsine and Diphenylcyano-arsine.—*G. T. Morgan & D. C. Vining, J.C.S.*, June 1920, 777.

The Action, Prevention and Treatment of Mustard-Gas Poisoning.

It is generally thought that dichlor-ethyl-sulphide $S < \begin{matrix} \text{CH}_2 & \text{---} & \text{CH}_2\text{Cl} \\ \text{CH}_2 & \text{---} & \text{CH}_2\text{Cl} \end{matrix}$ acts as intoxicant by undergoing hydrolysis giving hydrochloric acid. This is shown to be incorrect, the sulphur atom being the active principle, and the drug is toxic owing to adsorption between it and the protein particles. Exposed parts of the body should be treated with zinc ointment or bathed with a lotion containing aluminium and lead acetate.

In the treatment of mustard-gas poisoning painful lesions are dressed with any soothing application and manganese butyrate is injected. It was found that in some cases where the protein particles have agglutinated and fixed adsorbed constituent more firmly dispersion is better achieved with manganese ortho-coumarate or with manganese naphthylamine sulphonate, or with thiol-iminazolyl-ethylamine.—*J. E. R. McDonagh, Brit. Jl. of Dermat. and Syphilis*, Feb., 1924.

The above information is additional to that in Vol. I., p. 1101 and 1102.

Sulphuretted Hydrogen.

The gas is formed when organic matter decomposes. Cause of fatalities in sewers, occurs in mines, and is an ever-present danger in certain chemical processes. If concentrated, it may resemble Carbon Monoxide in rapidity of action, the subject appears to drop almost instantaneously. When in sufficient concentration to asphyxiate, the gas is odourless and only detected by a sweet taste. Authors consider it one of the most toxic of gases. Com-

parable to Hydrogen Cyanide in rapidity of action and concentration resulting in death. Even in concentration of 0.005 the gas is toxic.—L. i./24,347.

Haldane is convinced that it is unlikely that more poisonous gases (in chemical warfare) will be found than those which we now have, and that the respirators used in gas defence are adequate in protection. More probable is the development of skin irritants more unpleasant than Mustard Gas.—Jl. A.M.A. ii./25,1065.

Hydrocyanic Acid and Hydrogen Sulphide appear to be absorbed by the skin of some animals, whilst neither dogs nor guinea-pigs appear to absorb Carbon Monoxide through the skin.—Jl. Ph. & Exp. Ther., Nov., 25,324.

CARBON MONOXIDE AND DIOXIDE TESTS.

Frequent deaths have in the past occurred from Carbon Monoxide poisoning. Ordinary Coal Gas and Carbon Dioxide are also sources of danger.

WATER GAS and PRODUCER GAS are used for motive power of engines and for heating purposes, whereas for general lighting CARBURETTED GAS alone or Carburetted Water Gas mixed with Coal Gas is used.

PRODUCER GAS is made by passing air or a mixture of air and Steam through incandescent Coke or Anthracite Coal in a furnace generator, as in the Dowson producer. It consists of Hydrogen, Nitrogen, Marsh Gas and CO, with CO₂ as its principal impurity.

WATER GAS is made similarly, except that steam only is passed through the Coke, the product, being chiefly Carbon Monoxide and Hydrogen, $C + H_2O = CO + H_2$.

CARBURETTED GAS differs from both the above. It is made by passing water Gas made as above over heated refractory material charged with oils rich in hydrocarbons. The volatilised benzene and benzene congeners mix with the Water Gas.

Coal Gas contains 6-9% of Carbon Monoxide.

Producer or Water Gas 25-50%

Carburetted Gas 30%

The following test will indicate one part of Carbon Monoxide in 10,000 parts of the atmosphere. Even $\frac{1}{4}$ to $\frac{1}{2}$ % of the gas is most injurious, and if inhaled for some time may be fatal (Schmidt).

10 to 20 litres of air are aspirated for about 15 or 20 minutes through 10 Cc. blood (fresh), diluted 1 to 10 with water. The blood is then heated to the boiling point in a flask, and a current of air is passed into it which has previously passed through a 3% solution of **Sodium-Palladium Chloride**. The air, which passes out of the blood, is then led into bottles containing Lead Acetate Solution, diluted Sulphuric Acid, and another quantity of diluted Palladium Chloride Solution, in this order. *See also Iodine in Water.*

The presence of Carbon Monoxide in the air under examination is proved by the deposition of reduced Palladium metal in the last mentioned Palladium Chloride solution. A quantitative method on this principle is based on the fact that 106 parts of Palladium deposited are equal to 28 parts of Carbon Monoxide.

Note.—The blood used for the absorption of the Carbon Monoxide, is to be heated immediately after the aspiration with the air under examination, and the passing of the air is to be continued three or four hours.

The gas may also be detected by the aid of the spectroscope.

Detection of Carbon Monoxide in the Blood.

In addition to the spectroscopic method, **Kimkel's Colour Test** is valuable.

A pipette, 2 small test tubes, and a 3% Tannin Solution are necessary.—For details of method see Dix and Mann's Forensic Medicine.

Carbon Dioxide.—Haldane's apparatus is used for estimation in the air.

Nickel Carbonyl has caused degeneration of certain parts of the nervous system and produced death. Symptomatic treatment and purgation cured a case of nickel poisoning in a metal worker, caused by nickel dust being absorbed.

The poisonous symptoms are occasioned by the absorption of the nickel se free. The nickel is deposited over the surface of the lungs in a condition especially favourable for its absorption, probably as a hydrated sub-carbonate.

Antidote.—Oxygen.

For treatment of persons who have inhaled the noxious gases provide fresh air, sulphur baths, good food with Quinine and Nux Vomica; Chloroform Liniment with friction for local neuralgia and commencing neuritis.

Chlorine Inhalation and taken internally has been employed. Early and judicious use of this (by action of Hydrochloric Acid on Potassium Chlorate) should be successful.

Carbon Monoxide poisoning in the Senghenydd explosion.—B.M.J. ii./14,57

CARBON MONOXIDE POISONING in warfare and in blasting—useful chemical and medical notes:—

CO appears to be the toxic gas from the explosion of blasting charges, *e.g.*, Cheddite, Gelignite, Dynamite and Blastine. The usual symptoms of poisoning are headaches, dizziness and frequently vomiting. In the case of Dynamite, the CO present is due to faulty detonation.—W. J. Rutherford, L. i./20,184; JI. R.A.M.C., Feb. 1921.

Inhalation of Carbon Monoxide in coal gas a possible predisposing cause of pulmonary tuberculosis.—E. R. Hazleton, B.M.J. ii./23,763.

Carbon Monoxide poisoning from exhaust gases—two fatal cases. Less than a fifth of 1% of Carbon Monoxide in inspired air can cause serious poisoning. In streets of large towns with much motor traffic the mixture of Carbon Monoxide and other toxic gases, from exhausts, may have injurious effects on town dwellers.—B.M.J. i./24,338.

Carbon Monoxide poisoning in small garages, arising from running the engine in the confined space. 15 parts per 10,000 parts of air considered dangerous.—P.J. i./25,14.

Safety of gas fires, regarding CO. *Flueless* stoves appear to be the danger from the experiments cited.—B.M.J. i./25,611.

At Nauheim sensitive, anæmic, and debilitated subjects, brain workers and women feel tired and depressed near the effervescent springs, due apparently to the high content of Carbon Dioxide in the atmosphere. This is not so constant as generally supposed, since monthly weather reports some years ago showed that the proportion in London streets was sometimes 3 or 4 times as high on a working day as on a Bank Holiday. Cardiac cases derive benefit from the air near the springs in some cases, and many respond favourably to the effervescent baths. Other forms of disease, *e.g.*, tuberculosis, may be adversely affected by the stimuli.—L. i./25,1195.

PTOMAINES.

Under this name are classed a number of basic substances which are produced in meat, fish, and albuminoid food undergoing putrefaction by decomposition or by bacterial metabolism. They are akin to the alkaloids, several being poisons.

It has long been held that food-poisoning is in many cases due to ptomaines formed by the action of putrefactive bacteria, but actually there is **little to support this idea**. The poisonous compounds, such as Putrescine, Cadaverine, etc., are *late* protein degradation products, being formed when putrefaction has continued for some time, often weeks, at optimum temperatures. Thus, it appears that ptomaines are only formed when the food would be much too nasty to eat. Also, reports of toxicity of ptomaines have been exaggerated, being grounded on results of inoculating animals, whereas there appears to be *no direct evidence that feeding with ptomaines causes symptoms of food-poisoning*. At present it has not been established that putrefactive changes alone result in poisoning, and as a cause of extensive outbreaks putrefaction can certainly be excluded. In many cases, the food is normal in appearance and not tainted.—Food Poisoning, W. G. Savage. See also **Food Poisoning, Bacterial** this vol. p. 509, and **Botulism** Vol. I., p. 1039.

Symptoms of poisoning are those of gastro-intestinal irritants, but they may resemble those of Atropine poisoning. Dryness of the tongue, thirst, dilated pupils, debility, with probably rigors, offensive diarrhœa, high temperature and sickness with convulsions **may occur**.

Tyrotaxon occurs in stale cream, cheese, milk products; causes vomiting, purging, rapid pulse, dyspnoea, depressed temperature and prostration.

Antidotes.—Give emetics and Castor Oil, then stimulants. Amyl Nitrite, Strychnine, Digitalis, Caffeine, Sal Volatile, Tannic Acid, and Atropin hypodermically.

For **Fish poisoning** give Potassium Chlorate or Liquor Ammonia Acetatis, also Tinctura Capsici and Spiritus Chloroformi.

Outbreak of illness due to tinned meat in Carlisle. The meat (American Corned Beef) reported as bacteriologically unfit for food. It was proved to be contaminated previous to, or at the time of, canning in America.—L. ii./10,1613.

BACTERIOLOGICAL AND CLINICAL NOTES

with reference to Special Diseases.

[A Bacteriological Test Case is arranged containing the Apparatus, Stains and Solutions necessary for taking and examining Diphtheritic Scrapings, for detecting the *Gonococcus* in discharge, for staining Sputum for *B. Tuberculosis*, for collecting Blood for *Widal's Typhoid Reaction*, for the Gram separation of Organisms, for the staining of blood for Malarial Parasites, and for various other general clinical diagnoses.]

Acne Vulgaris.

(Obtain specimen by puncture and decompression of papule or pustule.)

A. Fleming (L. i./09,1035, B.M.J. ii./09,533) described the bacteriology of acne vulgaris. Gram positive organisms which, when seen in pus, are arranged very irregularly. In 44% of the pus films examined only acne bacilli were found. Acne bacilli with *Staphylococcus* were present in 53%. The acne bacillus stains less deeply than the cocci. The bacillus grows with difficulty on artificial media. A suitable medium for growing the organism was found to be Nutrient Agar containing 1 to 5% *Oleic Acid*. *Cultivation*.—Good results may be obtained by growing anaerobically in broth 3 weeks and then plating on Serum Agar with Neutral Red and about 2% *Oleic Acid*.

It can also be grown in deep tubes of 2% Glucose Agar,—the reaction of the medium being distinctly acid. Whitish colonies after three or four days at 37° C. appear which under a low magnification show a lenticulate shape. The relation of the bacillus to the suppuration in acne has been a matter of dispute.—M. & R.

Sudmerson and Thompson use an acid Serum Agar taking the deeper parts of the comedo in which the bacillus usually predominates, emulsify this in Saline and spread thinly on the slope so as to obtain colonies to pick off.

Cultivation from the comedo:—

T. H. C. Benians recommended for making Vaccines to grow simply in a tube of broth—the comedo being removed to same and then covered with Sterile Oil. *Staphylococcus Albus* will be present but is negligible—the bacilli out-growing these Cocci in about a week. The conditions are thought to resemble those in a sebaceous gland—L. i./13,1801.

In previous Editions of Vol. II., and in Vol. I., 19th Edition, p. 905, we have indicated that the name 'Bottle Bacillus' is synonymous with that of 'Acne Bacillus.' This should be corrected in the light of the recent work of J. M. H. MacLeod and G. B. Dowling (Proc. Roy. Soc. Med., Sect. Dermatol., 1928). The two are very different organisms. The Acne Bacillus is a true bacillus present in lesions of acne, and it may possibly be the cause, but according to MacLeod it is doubtful whether this has been definitely proved.

The *Bottle Bacillus* these workers have definitely found to be pathogenic and the cause of seborrhœic dermatitis. It is a yeast-like organism belonging to the group of the Fungi imperfecti, and is related to *Monilia*. The name should be discontinued and replaced by Spore of *Malassez*, or *Pityrosporon Malassezii*. It can be stained by the Giemsa method and is pleomorphic, the flask-shape being characteristic. Average size 3 to 7 μ by 2 to 6 μ . Grows freely on Maltose Agar at 25° C., Peptone Broth with 1% *Oleic Acid* and 1% Glucose added. It is almost universally present in the human scalp and has been cultivated by W. G. Garner since 1908.

For details of *Acne Vaccine* vide Vol. I., p. 905.

Actinomycosis.

A parasitic disease, due to the 'ray fungus,' first observed in cattle (wooden tongue), characterised by chronic inflammation, with or without suppuration, frequently resulting in formation of granulation tumours, especially about the jaws. Vide Potassium Iodide, Vol. I., p. 713 and 1030, for treatment.

To identify the fungus. 1. Place specimen, pus or sputum, in a flat glass dish on a black surface. Remove the characteristic yellowish particles if found, and carefully tease out on a micro-slide or cover-glass. 2. Fix film over the flame. Stain by the Gram-Eosin method.

The violet stained mycelium of the fungus as tangled webs or scattered branching filaments will be seen on a pink ground (leucocytes, epithelia, etc.), with a $\frac{1}{4}$ inch or even $\frac{2}{3}$ inch objective.

The "rays" may be observed without staining, but the stained specimens are confirmatory and valuable for reference.

Primary ovarian actinomycosis, a case of. Here the ovary was the primary seat of infection, and hence unique.—L. i./09,758.

Actinomyces vaccine suggested of strength 1 Cc. = 0.0001 Gm. Solid Substance as initial dose rising to 1 Cc. containing 0.001 Gm., repeated according to clinical symptoms.

A case, the result of chewing a stalk of corn, treated by Vaccine. Initial dose $7\frac{1}{2}$ millions, subsequently 5 millions—17 inoculations in all. Complete recovery.—J. Collie, B.M.J. i./13,991.

A case of Actinomycosis of the lungs.—B.M.J. i./12,302. Local lesion closely resemble tuberculosis.

Curetting with a dry swab as opposed to the use of a sharp instrument found satisfactory. Vaccine in dose of 25 million fragments once a week for a month. Four injections effected a cure combined with large doses of Potassium Iodide. The above dose of vaccine is larger than usually advised (3 to 10 million).—C. W. Dean, B.M.J. i./17,82.

Actinomycosis of the cæcum. On opening the abdomen a quantity of purulent fluid welled up (Actinomyces found). Potassium Iodide 50 grains thrice daily.—E. G. Slesinger, L. i./20,1220.

Actinomycosis, 23 cases. Promoted efficient drainage and curetted with a dry gauze swab. Vaccine therapy employed.—L. Colebrook, L. i./21,893.

Etiology. H. Wright's theory supported.—W. T. Warwick, L. ii./23,497.

A case of recovery with Iodine internally and intravenously. Patient's life despaired of on several occasions. Had great pluck and vitality.—A. Douglas Bigland and F. C. H. Sergeant, B.M.J. ii./23,61.

Ankylostomiasis (see also Vol. I., pp. 274, 422, 614, 810, 850, 876, 1032).—

The worm producing this disease (*Ankylostoma duodenale*) is about $\frac{1}{2}$ inch long and of a whitish colour. Its habitat is the small intestine of man. It attaches itself to the mucous membrane, and no fewer than 1,000 of them have been obtained from one patient. The male and female worm are quite different in formation. The eggs produced by the female pass away from the patient—as many as 8,000,000 have been delivered by a sufferer in a single day—and the small thread worm escapes from the egg. Mines afford an excellent hatching place for the young larvæ. Hygiene and sanitary measures are necessary to stamp out the disease.

The æmia it produces is probably due to toxins with a hæmolytic action.

Discussion on ankylostomiasis. Anæmia caused is frequently profound, producing ultimate death. Milk diet for a day or two, then Calomel and saline aperient; following morning Thymol 20 to 30 grains in a cachet, repeated twice at 1 hour's interval, with another Saline 2 hours after the last dose.—B.M.J. ii./09,1350. For further details on Thymol Treatment *vide* Vol. I., pp. 274, 810. Eucalyptus, Oil, p. 614.

According to the latest information Thymol is replacing Carbon Tetrachloride for hookworm.

LIFE HISTORY detailed, Mode of Infection, Duration of Infectivity. There are said to be two causative organisms. Most of the disease in the Southern regions of the U.S. and in Porto Rico was thought to be due to *Ankylostoma* (*Necator*, *Uncinaria*) *Americanum*, as distinct from the generally known *A. duodenale*. *A. Americanum* has not been identified in the Cornish mines. Where both species are abundant, individuals are often doubly infected. Methods of detecting eggs in fæces, *v. L. i./11*, p. 783. See also B.M.J. ii./09,775. Ankylostomiasis, Crusade against, in Bengal.—L. i./20,828.

Anthelmintics. *Efficacy as tested on earthworms.* (See also Vol. I, Carbon Tetrachloride, p. 274, Filix Mas, p. 422, Thymol, p. 810, Worms, p. 1098.

MUSTARD OIL is highly toxic (explaining the anthelmintic use of the allied onion and garlic).

COPPER SULPHATE also,—suggests its use in enemas against *Oxyuris*. The toxicity of this chemical is very high, being equalled only by Mercuric Chloride and surpassed by no other drug so far tried.

SANTONIN was found efficient.

Fresh PUMPKIN and "SQUASH" SEED are quite powerful and harmless anthelmintics. The active constituents are soluble in water. They are gradually destroyed by boiling. THYMOL was found active as also CHENOPodium OIL, Aspidium, and Betanaphthol.—T. Sollman, J1. Pharm. & Exp. Therap., Oct. 1918.

CARVACROL *p*-DIBROMBENZENE AND *p*-DICHLORBENZENE are suggested as anthelmintics. Absorption of the last two probably slight. Non-toxic.—*Jl. Pharm. & Exp. Therap.*, Nov., 1919.

Anthrax (for Antitoxin, see *Vol. I.* p.905).—*Bacillus Anthracis* was probably the first bacterium to be recognised, inasmuch as it was associated with splenic fever as long ago as 1849. It is responsible for 'malignant pustule' in man. If an animal die suspected of the disease the mode of examination is to cut off the ear and submit the blood from the same to bacteriological examination. The organism does not spore in the body of the animal, but if the air gain access, as in the case of an ordinary post-mortem investigation, the organism spores rapidly and hence becomes a grave source of danger.

The organism almost invariably occurs as long filaments, particularly in broth cultures (is non-motile). It grows on all the ordinary media both at room and body temperature, and produces in gelatin 'stab' cultures, typical 'inverted fir trees' appearance. By growing at 42° C. a non-sporing form can be produced, which is the mode of attenuation for the immunisation of animals, as introduced by Pasteur. The spores retain their vitality and pathogenicity for years in the dry condition. Martin has shown that the organism produces an alkaloid which is the fever producer and an albumose which induces the coma. The malignant diseases which the organism produce in man have been satisfactorily treated by **Sclavo's Serum** (*q.v.*) or by excision. If not diagnosed in time the organism may invade the blood stream, causing death, with symptoms of splenic fever, but the spleen is not so enlarged nor the bacilli so numerous in the organs.

Changes which occur in growth of the organism.—*B.M.J.* ii./11,1665.

Staining of the blood may be conducted by Gram's method (counterstaining with Eosin), also by Alkaline Methylene Blue. It is Gram positive.

Safranin—1 in 5,000 is stated to kill the spores of *B. anthracis* in 30 minutes.—*G. Salviola*, per *P.J.* i./23,547.

Anti-anthrax serum alone, *i.e.*, without surgical excision of the local lesion, is the treatment of choice. 50 to 100 Cc. are given intravenously, and the injections continued daily until temperature drops to normal. It is best to begin with 50 Cc. normal saline solution containing 5 drops of serum. Also of value prophylactically in 10 Cc. doses subcutaneously.—*A. E. Hodgson*, *L.* ii./28,594.

Appendicitis.—Common intestinal parasites seem to be associated with this disease, *e.g.*, *Ascaris lumbricoides* and *Trichocephalus dispar*. Chauvel has pointed out that appendicitis appears to be the most prevalent among meat-eaters, and notably beef-eaters. It is, on the other hand, unknown amongst Arabs or the Chinese. In religious communities in Brittany where meat is never eaten, appendicitis is unknown.

Disease of the vermiform appendix may be initiated more frequently than is commonly supposed by entozoa, *e.g.*, *Oxyuris Vermicularis* and *Trichocephalus Trichiurus* may prepare the way for bacterial infection.—*B.M.J.* i./10,42.

"Wisp" Bacillus found in septic wounds—a small slender Gram +, non-motile. In V-shaped bundles something like the diphtheroid group. Grows in the depths of an agar or glucose-agar "shake" or "stab." Obligate anaerobe. In civil practice found in appendix abscess cases or other suppurations from the intestines.—*A. Fleming*, *L.* ii./15,642.

Beri Beri. *Syn.* A form of **Polyneuritis**.—This disease infests the Federated Malay States and parts of China.

Etiology.—The disease is attributed to the consumption of white or "polished" rice. Vitamin B. deficiency is dealt with *p.* 102 and 111. No distinctive organisms have been found either in blood or urine.

Eyckman first brought forward (1897) evidence to establish a close connection between the polished rice and the incidence of beri beri. The characteristics in man which arise from degeneration of peripheral nerves (polyneuritis), *viz.*, paralysis, muscle atrophy, contraction of the extremities, have their counterpart in birds fed on milled rice. Feeding the latter with rice bran revives them.

Rice polishings comprise from 8 to 10% by weight of the original grain.

'Overmilled' would perhaps be a better term than 'Polished rice.' Rice thus 'polished' is deprived of pericarp, subpericarpal layers and embryo or germ. It does not occur in races using partly milled "cured" rice, and the poorly nourished are more liable to contract it than those well fed.

Treatment.—(See also Vol. I., p. 1035.)

In the Philippines a preparation of rice polishings called **Tiqui-Tiqui** is stated to be efficacious for children.

The addition of *Phaseolus Radiatus* fruits to rice has also been advised cf. Vol. I., p. 877.

The neuritis-preventing principle in rice polishings is insoluble in Ether, it is not inorganic, it is not volatile, but is destroyed by heat. It is absorbed by charcoal and cannot be recovered by water, Absolute Alcohol or Ether. Five Cc. of an extract equal to 5 grains of rice polishings were sufficient to protect fowls subsisting on polished rice, but $2\frac{1}{2}$ Cc. were not.—Review of Tropical Diseases.—Pr., Aug. '13, 218. See also Casimir Funk, B.M.J. i./13, 814, and H. Fraser and A. T. Stanton, L. ii./14, 398.

An adult accustomed to the use of polished rice would require 1.75 ounces of Polishings daily. The active substance is soluble in 91% Alcohol.

Liquid Extract of Rice Polishings, made with acidulated Alcohol of strength 1 Cc.=10 Gm. fat-free polishings. Another liquid Extract prepared more thoroughly was also tried (1=5). This contains less Alcohol in the finished product. Effectual in animal experiments (cocks). Dose for adult human beings 2 drachms. Rice Bran Powder in dose of 8 to 25 Gm. is also given.—A. T. Stanton, L. ii./12, 1005; see also L. i./14, 98.

The substance or substances in the polishings and in unpolished rice preventing beri-beri are soluble in Alcohol and are decomposed by Sodium Hydrate. Experimental proof.—H. Fraser & A. T. Stanton, L. i./15, 1021.

The **Anti-beri-beri vitamins** occur in the aleurone layer of the grain beneath the husk and in the germ of the grain. British flour owing to its excessive refinement, involving the almost complete removal of the aleurone layer with the husk, and also of the germ, is not protective against beri-beri. "**Atta**," Indian flour contains the aleurone layer and the wheat germ—this is protective against beri-beri. A mixture of the two used for our men. Yeast extract under the name **Marmite** also added to the British soldier's diet.—Sir W. H. Willcox, L. ii./17, 677. See also L. i./16, 553, and F. Gowland Hopkins, B.M.J. i./19, 507.

Tikitiki Extract, 20 drops every 3 hours, the usual amount given is not considered sufficient quantity and a dose of 3 Cc. every hour recommended. The extract may fail in infantile beri-beri if (1) disease too far advanced, (2) associated with broncho-pneumonia, (3) extract of inferior quality or dose too small.—A. V. Tupas, T.D.B., Vol. 19, 1922/757.

Rice in relation to beri-beri in India.

Although rice is the staple diet of millions in India, beri-beri is not widely distributed, its distribution as endemic being limited to a strip of coastal area in the Madras Presidency, part of Bengal and Assam, the coast of Burma and the valleys of the Irrawaddy and Salween rivers in that province. Although consumption of raw, milled and polished rice is as great on *West Coast* as East, beri-beri is *unknown* on the former but prevalent on the latter. As, in both, decorticated rice is the staple diet, it is clear that there must be some influence other than rice at work. 12,500 cases reported from endemic areas of Madras in 5 years, as compared with 102 in 21 years in non-endemic areas. In general, more raw milled and polished rice than parboiled rice is eaten by the people in the endemic areas, and it would therefore seem that the *distribution of the malady in Madras is associated with consumption of the former*, but many facts make it impossible to affirm that "beri-beri never appears when under-milled rice only is used," or that "beri-beri does not occur when parboiled rice is eaten." Although it is only within recent years that machine-milling of rice has been practised, beri-beri seems to have extended its endemic borders scarcely at all during the past 89 years. Out of 12,500 cases, over 2,000 were reported from districts where home-pounded (raw or parboiled) unpolished rice was in general use. Although not true of endemic areas of Madras Presidency that beri-beri never appears when under-milled rice only is used, it is true of the non-endemic areas. While under-milled and parboiled rices may, and do, afford protection against the disease outside the endemic zone, they do not always do so inside that zone. Amongst religious sects, the *Hindus*,

the greatest rice-eaters of all, are least afflicted with beri-beri, and the orthodox Hindu does not use parboiled rice, while other castes do. It would seem that residence in **an endemic locality** imparts to certain individuals a susceptibility to the disease which favours its development under conditions of life not sufficient to cause it in others not rendered susceptible by such residence. No satisfactory evidence that the malady is associated with storage or deterioration. Parboiling rice, while preserving much of its Vitamin B, involves considerable loss of Vitamin A. Pigeon experiments as to nutritive value show that raw unpolished rice is best, followed by raw paddy, parboiled unpolished rice, parboiled highly polished rice, and, worst of all, raw polished rice. Parboiled rice may be reduced, by washing, to the status of a raw milled and polished rice—few rices used in India are wholly devoid of Vitamin B. Rices known to have been habitually used by sufferers from beri-beri not by any means always those most deficient in Vitamin B. No strict parallelism between degree of Vitamin deficiency of rices and association with human disease. A rice potent to cause polyneuritis columbarum may yet not be associated with human beri-beri in places where it is known to be the staple diet of human beings. No pigeons fed on highly milled and polished rice developed beri-beri, but they developed polyneuritis. "There is no such thing in nature as a diet wholly wanting in Vitamin B, which is not at the same time imperfect in other respects." Possibility of overlooking the fact that foods are not only Vitamin-deficient but ill-balanced. Pigeon experiments show that beri-beri is caused by *insufficiency of Vitamin B* rather than by complete want of it. It is doubtful whether true beri-beri can be directly caused by Vitamin B deficiency, though it is an essential factor in the condition. *A poison may exist which imparts to polyneuritis columbarum the characteristics of true beri-beri.* This poison is probably peculiar to certain places, or is evolved in persons residing, or who have resided, in certain places, and its operation is rendered possible by the insufficient intake of a certain Vitamin or Vitamins in an otherwise ill-balanced diet excessively rich in starch and deficient in suitable proteins. One is not convinced that when arguing about the cause of "beri-beri" we are always discussing the same condition, as it was possible to produce in pigeons *no less than 4 distinct "beri-beri like" diseases*, by means of rices in common use. Further progress is necessary along lines separating these beri-beri-like states into recognisable entities, in order to determine causal factors in their production.—R. McCarrison, B.M.J. i./24,414,425.

A biochemical investigation showed that in human beri-beri and polyneuritis in animals the total fat content falls, the blood sugar content is high, the Calcium and Phosphorus contents are low, and there are marked changes in lipoidal products. The symptoms are suggested as being due to a disturbance of lipoid metabolism.—C. D. de Langen, per T.D.B. Vol. 20/23,391.

The B.M.R. in beri-beri patients was found to be the same as in normal controls. The respiratory quotients were normal and no evidence was found of damage to the excretory power of the kidney.—Jl. Trop. Med., April 1/24,78.

An epidemic of beri-beri thought to be due to cooking parboiled rice under steam pressure.—per Jl. Trop. Med., May 1/24,123.

B. asthenogenes, an aerobic saprophyte, capable of living anaerobically, cultivated on polished rice, produces free acid up to 1% ; if the acid produced is continually neutralised 22% can be obtained, chiefly of Propionic Acid. The effect of *B. asthenogenes* infection, in young pigs fed on polished rice, is to cause ulceration of the stomach due to Propionic Acid. Results of fermentation profoundly modified if husks and rice are mixed in equal proportions, or if large amounts of protein food are present. Authors consider these facts should be considered with reference to beri-beri among human rice-eaters.—"Research on Beri-beri," P. Noel Bernard and J. Guillerm, Jl. Trop. Med., April 1/24,82.

BERI-BERI IN JAPAN. Half a million cases yearly, with average death-rate of about 10,000, *i.e.*, about 0.2 per 1,000 of population. Heat seems to facilitate onset of the disease, which chiefly affects infants and young adults. As the result of experimental feeding of healthy men of diets with a low content of Vitamin B, it was found that the incubation period of the disease was 7 to 19 days, with full development in 30 to 40 days. Onset accelerated by diets rich in carbohydrates. Treatment by large quantities of *bran*.—B.M.J.E. i./24,45.

Observations of an epidemic in Freetown Prison suggest that lack of exercise plays an important part in determining an attack of beri-beri, where the predisposing conditions of diet exist.—D. B. Blacklock, B.M.J. i./24,1047.

Spore-bearing forms of *B. subtilis* found on rice grains used by families suffering from beri-beri and epidemic dropsy.—S. R. Bose, L. i./24,1054. See also H. W. Acton and R. N. Chopra, I.M.G., Jan., '25, 1-18.

Beri-beri from a diet of raw starch.—E. J. Kepler, JI.A.M.A. ii./25,409.

For a further consideration of Vitamins and the Anti-neurotic factor, see Vol. I., p. 593 *et seq.*, and this Vol. p. 102, 111.

Blackwater Fever. *Syn.* MELANURIC FEVER.

Severe rigors generally at onset, bilious vomiting, hæmoglobinuria. Generally thought a form of malaria, but Manson places it by itself pending settlement. Analogy between this and the hæmoglobinuric fevers of cattle is striking.—Manson.

A case of malaria suffered from typical blackwater fever and had distinct pyrexial periods all differing as to plasmodia, fever and hæmoglobinuria. Some factor at work differing from the usual processes of ordinary malaria.—Prof. Ronald Ross.—L. i./11,585.

The ordinary antipyretics should not be used; sponging is generally sufficient.

A critical review of work in the pathology of Blackwater Fever with special references to hæmoglobinuria and the conditions in which jaundice has been observed.—Prof. W. Yorke, T.D.B. 19/22,631.

Technique of Blanchard and Lefrou for the discovery of pseudo-spirochætes in hæmoglobinuric fever. 10 Cc. of blood is drawn from a vein into a centrifuge tube containing 1 Cc. 20% sterile Sodium Citrate solution; this is shaken up to prevent clotting and is then centrifuged three times. After the first centrifuge of 10 minutes the corpuscles are thrown down, leaving the citrated plasma above. The supernatant plasma is drawn off into a second sterile tube and centrifuged for another 10 minutes, until there is a light red deposit consisting of red cells, leucocytes and blood platelets. The supernatant fluid is decanted into a third tube and centrifugalised for 20 to 30 minutes, till a white deposit is seen—this contains the spirochætes.—J. G. Thomson, JI. Trop. Med., Aug. 1/23,252.

The workers just referred to discovered a parasite *S. bilihæmoglobinuricæ* in the blood, which they assign as a cause. Prof. Blacklock of the Liverpool School Lab., Sierra Leone, injected into a healthy adult the blood of a patient suffering from the fever. The temperature of the patient at the time was 102.5° F. No ill-effects after 6 months. **The evidence is against a spirochætal or other specific organismal origin.**—B.M.J. i./23,1030. See also L. ii./23,1362; W. M. Hewetson, JI. Trop. Med., Dec. 15/24,333; G. C. Low, Trans. Roy. Soc. Trop. Med., Vol. 17, No. 3, June, '23, p. 201.

"Blackwater Fever" is not a disease *per se* but only a complication of a severe infection of malaria, which is made premature by the exhibition of a dose of Quinine larger than that usually taken. Its action on the large number of severely poisoned cells accounts for the explosive character of "Blackwater Fever." It should be called "Malarial hæmoglobinuria." Many cases of malaria occur with "Blackwater Fever," but no "Blackwater Fever" ever occurred in W. Africa without previous malaria. Malarial parasites can be found in more than half the cases both before and after the attacks. The presence of polychromatocytes (certain erythrocytes in certain malarial bloods, which have the characteristic of a peculiar bluish staining known as the condition of polychromiasia or polychromatophilia) is of great diagnostic value as to the presence of obscure malaria. For the production of the symptom or complication of "Blackwater" in Europeans it is not so much the question of the number of parasites, but of the amount of toxin set free, which, together with the poisonous effect of the Quinine on the polychromatocytes thus made, produces a quantity of Hb. in excess of what the body can deal with. This would explain why the intensity of "Blackwater" varies, since it *must vary directly with the amount and virulence of toxin operating, and to a less extent directly with the amount of Quinine.*

Prophylactic Quinine must be used scientifically. 5 grains is not necessarily a prophylactic dose, though a useful average, and a man with an attack of fever while taking this dose will only have a very mild attack. Any factor which impairs the body's efficiency may turn a not too severe attack of malaria

into one of malarial hæmoglobinuria.—W. A. Young, *Jl. Trop. Med.*, Dec. 1/23, 350.

Malaria parasites found on the day before onset in about 75% of cases; on the day of onset, in 50%; and on the day after onset, in about 20%. That Quinine can produce hæmoglobinuria is certain—two cases quoted.—J. W. W. Stephens, *Int. Conf. Trop. Am.*, '24, 123.

Hæmoglobinuric fever caused only by repeated and intense infections with pernicious malaria over prolonged periods and in the author's opinion the only parasite concerned as the true causal factor is *P. falciparum* (*Syn. Laverania malarix*)—morphology.—J. G. Thomson, *Int. Conf. Trop. Am.*, '24, 130. W. M. James thought there were few, if any, to-day who hold that blackwater fever is a clinical entity unconnected with malaria. He agreed with Thomson as to *P. falciparum* being the causal factor. The proportion of parasites on blood examination was remarkably constant, being 80% *P. falciparum*, 24% *P. vivax* and 1% *P. malaria*.—*ibid*, 136, 139.

Caffeine Sodium Benzoate intravenously twice daily, morning and afternoon, accompanied by large quantities of saline water hypodermically or intravenously good.—A. A. Facio, *Int. Conf. Trop. Am.*, '24, 144.

In spite of all the weight of authority behind it, the creed, in my opinion, **that blackwater fever is uniformly of malarial character requires more proof.** The peculiarity of the geographical distribution of hæmoglobinuria, which by no means coincides with that of malignant or subtertian malaria, makes me sceptical as to their invariably identical etiology.—S. M. Klages.

Blastomycosis.—Stoddard and Cutler reviewed the entire subject of yeast organisms producing pathological conditions.—Rockefeller Institute for Research, Monograph No. 6, 1916, *B.M.J. i./17,460*.

Botulism.

Food Poisoning (Bacterial).

Savage divides food poisoning outbreaks of bacterial origin—chiefly caused by flesh foods—into three classes. (1) Those due to Gaertner group bacilli—the great majority of the large outbreaks. (2) Cases of botulism—a small group due to *B. botulinus*. (3) Those due to toxic action of other bacteria, usually stated to be putrefactive bacteria, such as *B. coli*, *B. proteus*, but there is no clear evidence on this point.

Gaertner Group Bacilli. The Gaertner (or *Salmonella*) group is fairly distinctive and intermediate between *B. typhosus* and *B. coli* in the colon-typhoid group of bacteria, and is frequently called the Paratyphoid-Enteritidis group. They possess the following characteristics: short sporeless bacilli with rounded ends, motile, gram negative, grow on gelatin with white or translucent growth without liquefaction. Pathogenic members of this group, including *B. enteritidis*, *B. paratyphosus B*, *B. suispestifer*, have the property in the animal body of producing toxins which are remarkably heat-resisting. This accounts for numerous poisoning outbreaks in which no living Gaertner organisms were found—sterilisation killing bacteria but leaving toxins unchanged.

Differentiation of food-poisoning bacteria.—The sodium salts of citric, *d* tartaric, *l* tartaric, *m* tartaric, fumaric and mucic acids are useful in differentiating the salmonellas. The organisms vary in their power to decompose the sodium salts; all the acids mentioned yield insoluble lead salts, and by these two factors the members of the group can be differentiated with the exception of *B. enteritidis* Gaertner which is variable.—H. C. Brown and Co-workers, *L. i./26,117*.

Fermentation of salts of organic acids as aid to differentiation—original papers: *ref. Jl. of Hygiene*, XXIII, No. 1., Oct. 15/24.

Investigation of the Salmonella group, with special reference to Food Poisoning. The name includes the *B. Enteritidis* of Gaertner, the Paratyphoid A and B, *B. Aertrycke* (4 types), and *B. suispestifer* (including *B. paratyphoid C* and the hog cholera type), and *B. abortus equi*.—*B.M.J. i./25,373*. See also *L. ii./26,397*.

The bacteriological diagnosis of botulism.—*B.M.J.E. i./26,36*.

The use of certain carbohydrates and glucosides to distinguish members of the Salmonella group of food-poisoning bacilli.—F. Wokes and J. H. Irwin, *Brit. Ph. Conf.*, 1927, *P.J. i./27,747*; *C.D. ii./27,37*.

Food poisoning, affecting 308 of 730 inmates of Plymouth Workhouse and

Infirmity, apparently due to heat-resisting toxin of *Salmonella*, as no living food poisoning organism found.—L. i./25,1254.

B. botulinus is a large bacillus (4 to 9 μ by 0.9 to 1.2 μ), which sometimes forms short threads. It is an obligate anaerobe, slightly motile, with four to eight flagella. The optimum temperature of growth is 20–30° C.—spores are not formed at 37° C. It is Gram positive, but does not hold the stain strongly. The bacillus will not grow to any extent in the animal body, poisonous effects being produced by toxins excreted into nutrient material. The toxins—unlike those from the Gaertner group—are destroyed by efficient cooking. *B. botulinus* will not grow in media containing more than 6% Sodium Chloride, so that, in salting, a 10% solution of brine should be used.—From Food Poisoning by W. G. Savage. See also Food Preservatives and Ptomaines, this Vol.

Sporing aerobic bacilli are frequent in sound canned foods, but are unable to develop and remain as harmless spores. Obligate anaerobic bacilli are rarely present in sound tins, but were nearly always associated with obtrusively decomposed conditions in the tin. Nearly 62% of sound tins are not sterile, the worst offenders being crab and lobster.—Food Invest. Special Report, No. 11, Na., 110, '22,614.

Occurrence.

In 624 samples of soil, vegetables, fruit, feeding stuffs, etc, collected in California, the bacillus was found in about 30%, and, contrary to common assumption, more abundantly in virgin mountain and forest soils than in cultivated places. The bacillus seems to be a common soil anaerobe, but conditions under which it causes toxic symptoms in man have not been defined.—Na., 111, '23,95.

The **Symptoms of Botulism** are very characteristic, and strikingly different from those met with in ordinary food-poisoning cases. They are almost entirely referable to lesions of the central nervous system. Prominent conditions are those due to disturbance of digestive tract—thirst, feeling of constriction in the throat, dysphagia, obstinate constipation, and ocular symptoms. Symptoms usually appear 12 to 24 hours after eating the infected food.

Canned Food Poisoning.

Tins passed as sound often contain living micro-organisms in dormant state, becoming unsound when conditions favour vegetation of spores of proteolytic or fermentative micro-organisms. Specific bacteria associated with outbreaks of food-poisoning confined to the *Salmonella* group (*B. enteritidis* Gaertner and *B. ærtrycke*) and the *B. botulinus*, which are rarely found in canned foods imported into U.K. The *Salmonella* group has been responsible for 51 outbreaks of food-poisoning in the U.K. since 1882, 16 of which were due to the living bacilli and 27 due to undestroyed toxins formed before canning; 26 were caused by canned meats. In 10 out of 14 outbreaks 1919–22 the tins came from S. America, which supplies 53.5% of canned meat imported by U.K. 16 of the remaining outbreaks due to this group were due to salmon (infected with living bacilli, survivals from infection at place of canning) and 9 to other fish, crustacea or fruit. In the case of fish, contents of tins undergo, in time, maturation changes, which are considered beneficial rather than otherwise. Botulism is common in U.S. and Canada—84 outbreaks between 1906–20, comprising 319 cases with 206 deaths, all traced to tins of canned fruit or vegetables (the primary seat of *B. botulinus* is in the soil). Canning does not kill the spores in the fruit if already present. The spores, if scanty, will not produce sufficient changes to cause rejection of tins as unsound but will cause tins to be 'blown' and contents to have offensive odour; non-vegetating spores of bacillus not injurious. Discovery of a hitherto unrecognised bacillus, *B. pleofructi*, regarded as chief cause of spoilage of tinned fruit; non-pathogenic to guinea-pigs and mice, and coccoidal in form until it vegetates when it grows long and slender. Most tins of condensed milk are imported from U.S.—no sound tins of sweetened milk found to be sterile. Possibility of transmission of specific infectious diseases by canned foods negligible, as also is chemical contamination by absorption of tin. Vitamin A not destroyed by canning process, but Vitamins B and C are; diet of canned foods must be supplemented by Vitamin foods.—“Canned Foods in relation to Health,” W. G. Savage and R. F. Hunwicke, B.M.J. i./24,127.

B. Botulinus spores are highly resistant to heat.—Details *re* canning fruit, etc.—Y.B.P. 1919, 39.

Home-canning methods responsible for recent small outbreaks. Several

methods are employed, but sterilisation under pressure is the only one recommended. For such vegetables as peas, corn, string beans, spinach, asparagus, and root vegetables, and for meats, the various boiling water methods are very unsafe and should not be used.—Jl.A.M.A. ii./28,730.

Epidemiologic analysis of 425 outbreaks of food poisoning in the U.S.A., 1923-1925.—Jl.A.M.A. i./28,462.

For further details of Botulism, Antitoxin, etc., see Vol. I., p. 1039.

Bungpaggia.—A disease on the Gold Coast—a micro-organismal infection. Slides of pus show heavy infection of yeast cells. Painful tumours are formed in the affected muscles. It is thought to be caused and perpetuated by a yeast fungus in infected grain. The yeast cell is probably absorbed from the intestine in the same way as fat is by migratory leucocytes and thence into the general circulation.—C. R. Patton, B.M.J. i./16,483.

Cancer, Sarcoma, and other Malignant Tumours.

At the time of going to press for the *last Edition of Volume II* of our work, W. E. Gye and J. E. Barnard, working under the auspices of the Medical Research Council, claimed to have discovered the causal organism of malignant growths.

Although the virus is a **filter-passing organism** it has been rendered visible by the application of optical methods, and has even been photographed. The virus alone does not produce a tumour, but when injected with virus-free extracts of sarcoma-tumours a malignant new growth is produced, showing that the extracts contain a 'specific factor' enabling the virus to attack the cells. There is no species specificity so far as the virus is concerned, but the 'specific factor' shows a very strict specificity. According to these workers there are therefore two factors concerned in the aetiology of cancer: (1) a living virus—the extrinsic factor, and (2) a chemical substance produced by the cells—the intrinsic factor. The causal organism apparently is "in the air," but it does not appear to affect normal, healthy tissues. There is no suggestion that a cure for cancer has been discovered, but the observations 'may represent a solution of the central problem of cancer.' So far they have only been able to reproduce sarcomata. Long and complete papers by these workers were printed in the *Lancet* of July 18th, 1925.

Since that date the **Lead Treatment** has received marked attention under the guidance of Prof. Blair Bell and the Liverpool Cancer Research Organisation. Numerous specialists have reported on the clinical use of Lead compounds, and a concise résumé of their opinions in chronological order, from 1922 to 1928, is provided in Vol. I., pp. 372-374 and p. 1043.

What may be called the **Shaw Mackenzie Lipase Theory** or the **Sodium Oleate treatment** is also discussed in Vol. I., pp. 761, 763. The late Albert Wilson reported some success with the method (Vol. I., p. 761). The same worker held a strong brief for **Goat's Serum** on the grounds that that animal does not suffer from malignant disease and hence the serum may contain some chemical constituent both resistant and curative. Details are given in Vol. I., p. 1042.

It is convenient to divide the subsequent information under the following headings:—

REPORTS OF CANCER RESEARCH ORGANISATIONS (including some notable reviews published in the past).

RECENT GENERAL PAPERS.

DIAGNOSIS.

CANCER THEORIES.

FILTER-PASSING VIRUS (Discussion of Gye's work).

IRRITANTS IN RELATION TO CANCER.

DEATH-RATE AND STATISTICS ON EPIDEMIOLOGY.

TREATMENT, RECENT NOTES ON.

IMPERIAL CANCER RESEARCH FUND.

EIGHTEENTH ANNUAL REPORT.—**Cerium Salts** were found active in certain experimental conditions, but had no influence on growing tumours. Drew approached the problem by studying the rate of decoloration of dilute Methylene Blue solution by normal and cancer cells. Decoloration is much more rapid with the normal. Russell and Gye have suspended tissue emulsions in fully oxygenated defibrinated blood and measured the rate at which oxygen is abstracted on incubation at body temperature. The more rapidly growing tumours, with exceptions, absorb more oxygen than those growing slowly. Respiration in normal tissues is a fresh line of research in connection with cancer.—*Na.*, July 29/20,696.

TWENTIETH ANNUAL REPORT.—Attempts to determine whether **Vitamin A** deficiency has influence on growth of malignant tumours. *In vitro* culture of tissues. Tar experiments.—*L. ii.*/22,198.

TWENTY-FIRST ANNUAL REPORT.—**Tryptophane-deficient** diet in young rats caused hypothyroidism and complete disorganisation of the pancreas by œdema. There is a specific demand for Tryptophane on the part of certain cells, and as the result of an inadequate supply specific lesions with specific symptoms. The result of the Tryptophane deficiency confirmed the conclusion that **vitamins are not required** by either normal or cancerous cells for their growth or life.—*L. ii.*/23,1368.

TWENTY-THIRD ANNUAL REPORT.—The researches of Gye and Barnard were the outstanding event of the year; the Fund's Laboratory had undertaken to test the validity of the hypothesis. Dr. Gye's experiments had been conducted with material supplied by the Fund.—*B.M.J. ii.*/25,1015.

TWENTY-FOURTH ANNUAL REPORT.—Work had been continued on the validity of Gye's claims, and results confirmed the existence of two factors in the successful transmission of these tumours. It was agreed that an Annual General Meeting be not held in future but that the Annual Report should continue to be issued.—*B.M.J. ii.*/26,996.

TWENTY-FIFTH ANNUAL REPORT.—Drs. Cramer and Crabtree had visited Berlin on behalf of the Fund to investigate Prof. Warburg's **biochemical conception of the nature of cancer**. Warburg had found that tumour tissues were not only able to break down carbohydrates by normal respiratory processes, but also, when deprived of oxygen, can act like yeasts and split carbohydrate, so that Lactic Acid appears as a final product. Tumour tissues can employ both the oxidation and splitting processes, even when the supply of oxygen is not restricted. On this basis, a hypothesis of tumour origin from Oxygen deficiency had been erected.—*B.M.J. ii.*/27,998.

TWENTY-SIXTH ANNUAL REPORT.—From a comparison of the mortality statistics of other countries, Dr. J. A. Murray (The Director of the Fund) concludes that the incidence of cancer is determined by general factors, local factors determining merely the site at which the cancer develops. Work on the new fowl tumour, discovered by Dr. Begg in the Fund's Laboratories continues. The importance of the tumour which had been proved to arise from endothelial cells, lay in the specificity of the 'agent' or 'agents' responsible for its transmission, in that it restricts its activity entirely to endothelial cells. The view that the filterable fowl tumour is not a true malignant neoplasm but an infective granuloma cannot therefore be sustained. Experiments on the **effect of diet** on cancer showed that there was no reliable evidence which would indicate a casual relation between cancer and the absence or presence or the excess of any particular dietetic constituent. Prof. Heidenhain's belief in the **transmissibility of cancer** from animals to man prove to be based on error. With regard to the Warburg theory experiments showed that high aerobic glycolysis of cancer cells cannot serve to distinguish cancerous from non-cancerous proliferations; a similar phenomenon had been observed in the study of cellular overgrowths produced by virus infections. As to the therapeutic possibility of affecting cancer growth by varying the Oxygen pressure in the inspired air, this was found of no value, even within the limits of safety.—*B.M.J. ii.*/28,1018.

NINTH ANNUAL REPORT OF THE IMPERIAL CANCER RESEARCH FUND.—The increase of cancer is referable to certain anatomical regions and not to others,—thus in males the increase is almost confined to the alimentary canal,—especially the stomach, while in females it mainly affects the same system, stomach and intestines, although the breast suffers also. There would appear

to be no special feature in the 'soil' favouring the growth of cancer, for transplantable tumours grow as well in normal animals as in those in which they first appeared. Yet a spontaneous tumour can hardly ever be implanted into an animal in which there has arisen a spontaneous tumour. With regard to treatment, it has not been found possible to arrest growth of spontaneously arising tumours,—it is thought doubtful whether any real progress is to be made along these lines. Cancer is not 'catching,' and 'cancer houses' cannot exist. Heredity plays a part in the development of cancer of the breast in mice. At all age periods the disease was more frequent when the mother, or either grandmother, or all three, had died from cancer of this organ. Resistance has not been induced either with an animal's own tumour or its own normal tissue. A number of cases of natural healing of spontaneous malignant new growths had been observed in mice affected with spontaneous cancer.

THE FOURTH SCIENTIFIC REPORT OF THE FUND showed that a portion of cancerous tissue transplanted to another part of the same body grows readily while the attempt to graft it upon another individual is abortive or difficult. The cancerous overgrowth of tissue is usually, and perhaps exclusively, in some part of the body which has been subject to continuous irritation. Cancer of the generative organs has not increased at the same rate as that for other organs, and most of the increases affect the higher age-periods predominantly.

E. F. Bashford pointed out that the common virus cannot exist for cat, mouse, and rat sarcoma, nor yet for sarcoma and carcinoma,—out of a pure mesodermo-carcinoma, a sarcoma may develop in a certain number of instances. Embryonic mouse skin has extraordinary power of affecting a complete protection against mouse mammary carcinoma.

Seventh International Congress of Medicine (1913—London).

E. Freund (Vienna), stated that normal blood contains a substance which has the power of destroying cancer-cells. He had isolated the substance, a fatty acid, which is soluble in ether and does not contain nitrogen. It is not present in the blood in carcinoma, but in its place is found a substance which possesses the faculty of destroying the normally present fatty acid. His theory is that the deficiency and disappearance of the fatty acid must occur in advance of, and not as a result of, the growth of a cancerous tumour.

Clowes (Buffalo) had found that the virulence of tumours and their rate of growth are directly proportionate to the potassium content and inversely proportionate to the calcium-content.

Minute quantities of Radium present in most tissues,—much increased in cancerous tissue. Examination of gallstones (always associated with cancer) showed that while a mere trace of Radium is to be found in them in non-cancerous cases, 85 times as much is present in cancer of the bladder, and even when the cancer was elsewhere than in the gall bladder there existed an increase of Radium in the gallstones.

Radium can be removed out of solution by *Staphylococcus Pyogenes Aureus*. Bacteria form the common foci of gallstones. Possibly bacteria concentrate the Radium round themselves and so form foci of gallstones thus leading to cancer of the gall bladder.—W. S. Lazarus Barlow,—*L. ii.*/13,729,704.

INTERNATIONAL CONFERENCE ON CANCER, London, July, 1928.

Relative values of Surgery and Radiation. G. REGAUD (RADIUM INSTITUTE, PARIS), said that radio-sensitivity of cancer was extremely variable. Of the two different species of cancer of the cervix uteri, epidermoid (a stratified pavement epithelioma, showing structurally the morphological changes or manner of growth peculiar to the epidermis) and glandular, cures by selective radio-therapy had been obtained only in the former, due apparently to the activity and rhythm of division on the one side and the secretory function on the other. In addition, many factors independent of radio-sensitivity influenced the results of radio-therapy, *e.g.*, extent of primary cancer, its distant spread, its accessibility, and the radio-resistance of the intervening tissues and organs. Ray action could

be used on a small neoplasm where it was out of the question in a more extensive one. None of the methods of treating cancer could promise uniform success.

Cancer of the cervix uteri. M. DONALDSON (St. Bart's.) gave the following grounds for definitely deciding in favour of radiation as against hysterectomy—(1) the negligible mortality with radiation, (2) statistics of survival-rate in no way inferior, (3) with improved technique, more patients will seek early advice, with consequent improved results, (4) it will bring into general treatment radiotherapy in incurable cases, (5) it will encourage the younger gynaecologists to adopt a method of treatment which they will be able to carry out more successfully than the difficult Wertheim's operation. W. P. HEALY (New York). The most important determining factors in prognosis were the clinical stage of the disease and the radio-sensitivity of the tumour, and, when surgery was employed, early diagnosis and the degree of malignancy. COMYNS BERKELEY (London), gave figures relating to the radical operation. He considered that if the glands were carcinomatous the immediate operative mortality was raised from 12 to 20·6%. VICTOR BONNEY (London) thought a five-year survival period not enough—10 years should be taken before absolute cure was claimed.

Cancer of the rectum.—SIR C. GORDON-WATSON described his method of approach by open operation through the perineum, with Radium barrage per vaginam and Radium in bulk in the lumen of the rectum, employing Radium salt in platinum needles. The future of successful radiation of cancer tissue depends on the possibility of giving an optimum dose—at present empiricism is the main guide. J. P. LOCKHART-MUMMERY. When operation is performed under the most favourable conditions the mortality is about 3·5% and cures, on a 5-year basis, are 50%. The best method of treatment is operation: the prospects of cure are good, and where operation is possible the substitution of radiation is not justified.

Cancer of the breast. PROF. BURTON LEE (Cornell University). Irradiation in conjunction with conservative surgery had justified itself. Other speakers were in agreement with this view.

Cancer of the buccal cavity. DOUGLAS QUICK (New York) Radium preferable to X-Rays. Filtered Radon 'seeds' employed with good results. Applicators within the mouth were of no value. STANFORD CADE (London). Surgical treatment had given results so indifferent that those obtained by Radium appeared brilliant. In an operable growth the choice should be local excision with the diathermy knife and subsequent irradiation of the scar.

Etiology. JAMES EWING (New York). The older physicians were probably correct when they said that cancer of the mouth would probably disappear if tobacco, bad teeth and syphilis could be eliminated. It seemed clear that cancer only arose on tissue altered by chronic irritation. There was no one exciting cause of cancer nor one great secret in the cancer cell. A. LETCH (London Canc. Hosp.) negatived the claim of Gye and Barnard. He thought

the 'growth substance' might yet come within the range of experimental investigation. A. BORREL (Strasbourg) pointed out that the cancer age coincided with the age of the whitening of the hair, when the trophic system became a phagocytic system. J. B. MURPHY (New York). The real nature of the cancer agent seemed at least to be emerging. The indications were that one had to deal with an endogenous chemical substance rather than with extrinsic living viruses. The parasitic theory of cancer formation he considered highly improbable. J. McINTOSH (London). If a virus were so small that it could live and multiply in the interior cells it was well situated for influencing such cells. The virus theory had been regarded too lightly. PROF. BIERICH (Hamburg) referred to the accumulation of Lactic Acid in cancer tissue. All cancer tissue was rich in the acid, which invaded neighbouring tissues breaking down barriers which might have hindered the progress of the disease.

Medicine and Diagnosis. SIR THOS. HORDER. Even when the growth was inoperable the treatment of the cachexia must be paced and life prolonged without adding to the patient's discomforts. The wave of enthusiasm for a fruit and vegetable diet was not justified, patients at the Cancer Hospital did better on a mixed diet. Radiation undoubtedly relieved cachexia in some inoperable cases.

Occupational Cancer. J. C. BRIDGE and S. A. HENRY (Home Office). Cancer, in order to be classified as of industrial origin, must fulfil two conditions: (1) that the incidence rate in that occupation exceeds that of the general population to a significant extent; (2) that in the occupation there is sufficient association of the worker with a substance proved to have carcinogenic properties. There was only one effective method of prevention—substitution of innocuous bodies. A binding substance, non-carcinogenic to animals, had been invented to replace pitch. T. H. C. STEVENSON. The carcinogenic influence of Alcohol appeared to be less than that of syphilis, though both cause increased cancer mortality and point to the rule of a 'godly, righteous, and sober life' (this may explain the relative escape from cancer of the clergy). O. ROSTOSKI and G. SCHMORL (Dresden). Schneeberg lung cancer—a pulmonary affection due to malignant tumours of the lungs, found in the Bismuth, Cobalt, and Arsenic-mining district in Schneeberg.

Radiology. C. REGAUD (Paris). Given the same quantity of radiation with X-Rays earlier and more marked effects were produced when the dose was given in shorter periods than when spread over a longer time. These remarks were confirmed by R. G. CANTI (London).

Chemotherapy. PROF. BLAIR BELL. In the synthetic preparation of a chemotherapeutic substance, *e.g.*, a Lead complex, not only should the specific agent in regard to growth and the malignant cell be considered, but also the special chemical constitution-function of the tissue in which the neoplasm has developed, and if it were possible to make a Lead preparation absolutely specific for any one

type of malignant growth it would appear that that preparation should vary according to the original tissue from which the neoplasm had sprung. It had been found that Lead was detrimental to the cancer cell and the effects of radiation were augmented by the previous use of Lead. There was considerable evidence to support the view that by itself Lead, even in the crude preparations now used, could cause disappearance and apparent cure of malignant neoplasms and could sometimes beneficially effect leukaemia and other neoplastic conditions. PROF. W. J. DILLING said the successes obtained by Lead treatment were greater than could be explained by spontaneous arrest or other causes. He expected a substance to be hit upon more effective than Lead—but he did not expect a panacea. The aim was to find something which would retard the progress of the malignant cell without damage to surrounding tissues. BASIL HUME. Results with the Lead treatment at St. Bart's. had been highly unfavourable. Cases so treated only lived for an average of 13 weeks, which was much less than their average expectation of life had they not been so treated. Grave health commenced in several as soon as treatment begun. STANLEY WYARD concluded that Lead was of absolutely no value. A. P. THOMSON treated 55 cases, with favourable influence in 15, but improvement was only temporary. Colloidal Lead better than Lead Glycine or Colloidal Lead Phosphate. PROF. BLAIR BELL replied to the criticisms and said that it was at present admittedly a crude treatment. DR. PELCZAR (Cracow) referred to research into the action of certain lipoids and albumins and the diminution of tumours following their injection. SIR THOS. HORDER in closing the discussion said that the differences in results with the Lead treatment were possibly in part due to differences of technique, but no remedy was of practical value where the margin of safety between its lethal effect on the vital tissues and the resorptive effects upon the growth was less than that which admitted of reasonable control. He felt that the preparations of Lead at present available had not yet arrived at the point of safety to enable them to advise their patients in this direction.

Early Recognition and Treatment of Cancer of the Stomach. SIR BERKELEY MOYNIHAN stated that there were no symptoms pathognomonic of carcinoma in any of its stages; the symptoms were only suggestive and not conclusive. The success of medical treatment in early cases was one of the causes of the very high mortality—instead of seeking to subdue symptoms one should seek to evoke them. Examination by the radiologist, and by the chemist for blood in the faeces must be insisted on. A. F. HURST. Achlorhydria was not the result of carcinoma of the stomach but preceded its development. Many cases of achlorhydria were due to chronic gastritis which was found present in almost all cases of carcinoma of the stomach. A. J. WALTON. The hope for greater success lay not only in a wider recognition of the early symptoms, but in a subsection of chronic ulcers in patients between 40 and 60 instead of prolonged medical treatment. D. P. D. WILKIE. The employment of a Barium meal X-Ray examination in all cases of obscure

ill-health would reveal early cases of carcinoma when present, though clinical signs and symptoms were still indefinite. PROF. R. BASTIANELLI (Rome) thought it no exaggeration to say that with the most hopeful surgical technique it could not be expected that more than 7% of patients with stomach cancer were likely to be cured. T. IZOD BENNETT (London). A carefully performed gastric analysis yielded a reliable diagnosis in more than 90% of all cases. PROF. E. C. DODDS (London). The lack of mention of the Abderalden reaction was an indication that it was dying the death it deserved. The *Shaw-Mackenzie reaction* and the *Ringold method* had both proved non-specific. SIR WM. WILLCOX said it was well to remember that one of the early signs of cancer of the stomach was a rapid falling off in the ferment activity, and that the percentage of inorganic chlorides was much increased.

The effects of Radium and X-Rays on the Blood-vascular and Lymphatic Systems. A. LACASSAGNE (Paris) considered the death of cancer cells was brought about by the direct action of radiation on the cancer cells themselves. CLIFFORD MORSON (London). A very large dose of Radium could cause extravasation of blood, while a smaller dose caused obliteration of the lumen without rupture of the walls. The greater the vascularity of the organ in which the tumour was growing the better the results from the application of rays. DR. PFAHLER (Pennsylvania) was convinced that fibrosis, telangiectases and necroses were the result of cumulative effects of X-rays rather than of a single massive dose. ROBERT KNOX (London). Systematic blood counts should be made. A drop in the number of lymphocytes was an indication to 'go slow' with radiation treatment.—B.M.J. ii./28,105-109,165-173.

Manchester Cancer Campaign.—Increase in cancer a definite fact in most countries. Enormous preponderance of cancer incidence amongst cotton operatives. *Mule-spinner's disease* one of the most favourable types of malignant disease as it can be detected early and cured by radical removal. Cancer produced in mice with the lubricating oil actually used in cotton mills—shale oil more liable to produce cancer than shale-free petroleum oil, and lubricating oil made from sperm oil is quite harmless. Samples of toxic oils treated with Sulphuric Acid rendered quite harmless. Spread of a tumour regarded as evenly centrifugal and glands not likely to be affected other than by peripheral permeation—no operation truly radical unless the tumour, a wide area round it, the lymphatic trunks of the areas, and the lymphatic glands are removed. Pre-existent ulceration not an important factor in cancer of the stomach. Radium probably the best form of treatment for cancer of the tongue, rodent ulcer, and epithelioma of the skin. The use of Radium and X-Rays gave 10% of apparently permanent cures in inoperable cases. In carcinoma of the cervix 30% of inoperable cases were cured, but 15% of these occurred later. When cancer of the breast is treated in the early stages by surgical methods the outlook is very hopeful, over 80% being alive 10 years after operation. When axillary glands are involved treatment offers three years of life to 50%, 5 years to 33.3%, and 10 years or more to 20%.—B.M.J. ii./28,68.

British Empire Cancer Campaign.

In a report on Cancer Research in the U.S., Dr. A. Leitch said that American workers had in the main failed to agree with the Gye theory—and it was evident that here at home scientists as a whole had failed to accept it as conclusive.—B.M.J. ii./27,112.

Ministry of Health Report on Cancer of the Uterus (No. 40).

For the cure of the disease treatment by Radium is almost as efficient as abdominal hysterectomy. This conclusion is based on reports from Germany, Austria, America, Sweden, France, Switzerland and Belgium. England is conspicuous by its absence from the list—referring to this Sir George Newman remarks: '*One is impelled to enquire whether these remedial agents, Radium and X-rays, are used as widely as they should be and with similar results in England.*' The percentage of operative mortality for abdominal hysterectomy was 17·3 and that for Radium nil. The survival rates (5 years) for abdominal hysterectomy and radiation respectively were 18·3 and 22% for all cases, and 37·6 and 35·8% excluding inoperable cases. Radiation has the further advantage than in inoperable cases it can show a survival rate of 12·7%.—B.M.J. ii./27,228.

A Supplementary Report (No. 47) based on the records of 1,000 cases at the Samaritan Free Hospital from 1901–1926 gives operative mortality for cancer of the cervix of 8·6%, the survival rate being 43·8 for 5 years and 36·6 for 10 years. These figures indicate that the results of English surgery are if anything better than those of other countries. An interesting point raised is the possible association of cancer of the uterus with miscarriage. It seems evident from the figures that the early termination of pregnancy before the foetus is viable has a definite association with the occurrence of cancer of the cervix.—B.M.J. i./28,69; see also Min. of Health Memorandum, *ibid* 24.

Ministry of Health Report on Cancer of the Rectum (No. 46).

A survey of the literature embracing 10 countries and concerning nearly 6,000 cases. An average period of 12 months elapsed between occurrence of the first symptoms and the patient coming to operation; rather less than half the cases seen were operable; one-sixth of the cases undergoing radical operation died as a result, the mortality in patients in an advanced stage being higher; two out of five were alive 3 years after operation. On the average radical operation prolongs the life of a patient by 0·9 years.—B.M.J. i./28,110.

The League of Nations Cancer Inquiry.

From a study of the cancer statistics of England and Wales, Holland and Italy, the Sub-committee is satisfied that **childbearing does not predispose the woman to cancer** of the breast and uterus. The higher incidence of cancer of the uterus upon married women is the consequence of the immediate effects of a single parturition, and women who have borne many children are less rather than more, liable to cancer of the uterus than married women who have borne few children.—B.M.J. i./26,161.

League of Nations Cancer Commission—1923–1927.

'Much must yet be done before attempts to appraise "racial" elements in the prevalence of disease can be successfully undertaken.' The Commission concludes that on the one hand early operation is a far more successful measure than even the general body of the Profession supposes, and on the other that the frequency of resort to operation remains 'deplorably low.' As to the influence of fertility, they find that a fertility below the normal for any particular nation is associated with increased liability to cancer of the breast.—B.M.J. ii./27,1157.

Public Action in regard to Cancer.

In England one is conscious of its patchwork, its incompleteness, and even its inconsistencies and overlaps. Compared with some efforts in the U.S.A. with the 'centres anticancereux' of France, or with a State Cancer Institute as in Milan, it may seem meagre, but it has in it the elements of elasticity and capacity for development.—Sir George S. Buchanan, L. ii./28,163. We agree there appears to be overlapping and absence of concerted action.—W.H.M.

The Cancer Cell.

The living cancer-cell is the essential part of every cancerous growth, for when the cell dies it is impossible for any of the parts, agencies, or faculties of cancer to be excited or developed. In a successful graft the centrally placed cells die, but the peripheral portion of the transplanted tissue excites the surrounding fibrous tissue to form a support (stroma) for the tumour, whose soft

issues are wholly developed directly from the implanted living cancer-cells of the graft. A study of the cancer-cells demonstrates that it is only a variation of a normal cell, for it possesses neither in structure nor in power anything not found in the healthy cell. Cancer-cells possess a power of continuous multiplication, retaining inherited limitations to type of cells among which they first appear, but they develop and differentiate but little and irregularly in a manner neither purposeful nor effective.—B.M.J. ii./11,766.

A disease that generally arises in cells that are growing old, thus in woman the breast and uterus are prone to cancer as they get old before the rest of the body. The different incidence of cancer in the two sexes is the result of the special liability to the disease of organs possessed by one sex only. A chart showed the close parallelism of the cancer curve, in woman, and in their generative organs only (at 40 to 50 years of age), and the near approach of the curve for women, when we exclude disease of their generative organs, to that of men (at 50 to 60). Age, chronic irritation, x-rays, alcohol, are conditions that deteriorate the evolution of the individual cell.—Sir Alfred Pearce Gould, B.M.J. ii./10,1836; L. ii./10,1665; B.M.J. ii./12,129.

The methods suggested by various workers for serum diagnosis of cancer had yielded negative results. Histological types comprised the majority of forms met with in man. Frequency of primary carcinoma of the liver associated with cirrhosis and primary malignant growths of the suprarenal was of interest.

Mice immunised subcutaneously by injections of tumour or of normal tissue are resistant to the implantation of cancer in internal organs. The immune state is one of general distribution throughout the organism and not of local occurrence at the site of the immunising inoculation.—L. ii./11,92.

A fragment of cancer tissue transplanted to a previously normal mouse produced an increase in the amount of physiologically active Hydrochloric acid during digestion. Mice which had been apparently completely protected against the inoculation of cancer had developed the disease spontaneously. Prevention of all who die from cancer is essential.

Plimmer's bodies, which were considered peculiar to cancerous tissues, are also present in healthy reproductive tissues. This disposes of the idea hitherto held that Plimmer's bodies are parasitic organisms.

Recent General Papers.

In the discussion of a paper on the "Causation of Cancer," by SIR WM. BRUTHNOT LANE, SIR ARTHUR NEWSHOLME, while admitting that the theory, of intestinal stasis as the cause of cancer was 'feasible, ingenious and useful, queried why there was much more intestinal cancer in the male than in the female, and considered it difficult to explain by that theory why in certain communities chronic constipation associated with toxic absorption leads to large increase in cancer of the breast, while in other countries there is more cancer of the uterus. Significant that in child-bearing women cancer of the uterus is more common than in single women and *vice versa* in the case of cancer of the breast.—Int. Conf. Trop. Am., '24, 753, 759. The author in reply said that the cause was obviously traumatic.—*ibid.*

Breast disease in England is often associated with the presence of an acarus, the *Demodex Folliculorum*, at the orifice of the nipple. It lives deeply in sebaceous glands and is not killed by skin antiseptics. Confirmation of the work of Borrell, who suggested that the parasite may cause malignant disease.—H. Chambers and A. M. Somerset, L. i./25, 172. and 361.

Describing cancer as due to cellular anarchy mistakes effect for cause; it is better to say that cancer commences as cellular disorientation. All organic functions being regulated by the nervous system, this system should be regarded as the origin of all derangements of function. A systemic reaction so profound as that produced by cancer cannot be due to a group of cells being in a state of anarchy. Traumatism in general, and chronic ulceration in particular, should be regarded as extending beyond the limits of organ or region, and as affecting simultaneously all the regional nerve supply.—J. Thomas, La Vie Medicale, B.M.J. E. i./25, 82.

It is useless to look for the cause of malignant disease in the growth itself, and the existing cause (which the author calls 'X') will eventually be found either in the blood or carried by the blood—probably some minute biochemical change affecting *reaction of the blood* on certain types of cell, cells that have suffered from a source of irritation or which are undergoing degenerative changes at end of natural functional activity. The only

cases of malignant disease in which cure can be hoped for are those with a radio-insensitive growth, absence of the underlying cause ('X'), and complete extirpation. With radio-insensitive growths the chances of life are not increased by radiation but are diminished if radiations are carried to the extent of interfering with natural resistance of tissues.—A. E. Barclay, J.I.A.M.A. ii./25, 1715.

We lack to-day adequate data to decide absolutely whether civilisation and culture constitute cancer-predisposing or merely cancer-revealing influences. Statistics fail to answer the problem of the incidence of cancer, owing to defective working base. Defective diagnoses may be made by physicians. Statistical bureaux lack scientific, medically trained leaders, and the medical world shows little interest in statistics.—S. Peller, per J.A.M.A. ii./25, 1731.

A Method of Cancer Research.

A plea for the Cartesian method of research based on deductions from the known facts concerning cancer. From this deductive process the writer concludes that cancers are cells that have entered upon the degeneration of old age too soon and are being nourished by the juices and stimulated by the hormones of the younger and more vigorous tissues round them. Cancer cells are not young or progressive, but senile, regressive, and decadent. They are embryonoid, not embryonic, and for this reason they multiply incessantly and uselessly. Following the deductive process, he shows that the same forms of stimuli which act at one end of the developmental cycle to start a proliferation of progressive type ending in the formation of the normal human embryo, are capable of acting at the other end of the cycle to produce the embryoma-like proliferation of regressive type termed cancer, embryos being the tumours of the beginning of development, cancers being the embryomas of the end of development. With regard to predisposition, he concludes that everything promoting degeneration in general is potentially a predisponent, *e.g.*, the inadequate use of important organs, such as the reproductive organs of woman or the digestive organs of both sexes. Finally, cancer is a **cluster of cells** which owing to over-stimulation and more diffuse degenerative influences are **finishing their cycle of development too soon**, structure and function approaching the original simplicity and the primitive faculty of reproduction coming to the fore. Under the fertilising influence of the reproductive stimuli these cells burst forth into an embryonoid or amœboid reproductive activity and find their way along the lines of least resistance to all parts of the body.—H. Gilford, L.i./26, 858–862.

Rous chicken tumours capable of infecting by cell-free filtrates can be destroyed by β radiation. Chickens in which the tumours have thus been made to disappear exhibit resistance to subsequent infection.—J. C. Mottram, L. ii./26, 1266.

Cancer and how to fight it.

In the last 70 years the mortality from cancer has increased fivefold, and this despite the fact that more people than ever are being cured. The operations for cancer are now reaching their limit and no considerable change can be expected. The only hope is in the education of the public to seek advice in early stages, and in research work. It is important that the public should know (1) that cancer is always at first **a local disease**, (2) that it attacks diseased rather than healthy organs (*i.e.*, **a high standard of health should be aimed at**), (3) its occurrence is influenced by antecedent conditions, *e.g.*, **chronic irritation** (4) it is not hereditary, is not caused by certain foods, or lack of same, and there is insufficient proof that "cancer houses" or "districts" exist, (5) it is neither infectious nor contagious, (6) it spreads by direct extension, *i.e.*, it never begins as a generalised systemic disease, (7) it rarely causes pain in the early stages; the existence of carcinoma is compatible with perfect health, (8) while the disease is local and the growth accessible cancer is curable.—Sir Berkeley Moynihan, B.M.J. Supp., i./27, 29.

On the nature of immunity to implanted Malignant Tumours.

Immune animals inoculated with any transplanted tumour produce antibodies toxic to a wide range of malignant growths. The serum alone, in the case of an animal immunised against a heterologous tumour, is lethal to in vitro cultures of the antigenic tumour when sufficient complement is present, but the serum of an animal immunised against an homologous tumour only

kills cultures of the antigenic tumour in the presence of leucocytes appropriately conditioned, or of some secretion from the latter. Thus, any malignant cell growing in a rat is, in the absence of leucocytes, quite undamaged by antibodies present in this or any other rat's serum. Leucocytes only form their special cytase when extravasated, partial anaerobiosis probably being the determining factor.—T. Lumsden, L. i./27,122.

Diagnosis.

The role of fat in the etiology of cancer.—It is possibly the tissue which plays an important part both in the etiology and certainly in the progress of the disease. Note the pigmented condition of the fat in some cases of carcinoma *p.m.* In operating on mammary cancer the oily and fluid state of the circummammary fat is very noticeable. In those cases where oophorectomy for inoperable mammary cancer produces disappearance of outward signs of the disease there is improvement in general health and increase in subcutaneous adipose tissue. **Chemical Examination of Fats.**—normal human and cancerous, gave interesting data. The fats were extracted by heat and examined for Iodine Nos. with Wij's Solution—there was decided difference in human fat before and after puberty—44.477 average Iodine Value (a measure of the non-sat. fatty acids) between 9 and 11 years, and 60.88 between 16 and 19. Fat in health gave average Iodine value 62.1 and in cancer patients 72.62. Protoplasm viewed as an emulsion of proteins and lipoids, *i.e.* there are cell fats, and any causes that make them more fluid lead to degeneration and destruction. What effects an excess of non-saturated fatty acids in the cells of adipose tissue of a part may have on surrounding somatic cells must be a matter of conjecture.—L. i./11,1560.

Predisposing causes, how cancer commences and spreads, and diagnosis.—J. Rutherford Morison, B.M.J. ii./19,659.

Recognition of Cancer of the Stomach.—Stress has been laid in the diagnosis of carcinoma of the stomach upon the *absence of free Hydrochloric Acid* and diminution of the total acidity of the gastric contents removed after a test meal—there are, however, so many exceptions that too great importance must not be attached to it. In chronic gastric ulcer and in carcinoma, originating in chronic ulcer, free Hydrochloric Acid is usually present in about normal amount—sometimes slightly in excess, and the total acidity corresponds. In old standing cases which may be chronic ulcer, or may have overstepped the line and become malignant, no information of value is given. In chronic gastric ulcer, apart from growth, very rarely, in carcinoma of other organs commonly, and after severe hæmorrhage, free Hydrochloric Acid may be absent. These exceptions to be borne in mind in considering the value of absence of free Hydrochloric Acid and diminution of total acidity.—B.M.J. i./11,1458. Cf. Stomach Contents Examination, this Volume.

Oleic Acid method of diagnosis of Gastric Carcinoma.—

The amount of Hübl's Iodine Solution, necessary beyond the normal limits, operating on gastric contents after a trial meal, indicates Oleic Acid.

One of the early signs of cancer of the stomach is a rapid falling off in the **ferment activity** and the percentage of **inorganic chlorides** is much **increased**—Sir W. H. Willcox.—B.M.J. ii./28, 105.

Reaction of the blood serum as aid in diagnosis of cancer.—

Titration using Dimethylamido-azo-benzene as indicator. The results show that some sera are more alkaline than others.—B.M.J. ii./13,780.

Iodophil Reaction. Colour reaction with Iodine which occurs in certain conditions in certain epithelial and cancer cells. Some relation to Glycogen.—C. J. Bond, B.M.J. ii./21,973, *et seq.*

Explanation of high blood sugar curve in malignant disease is not clear, but it is possible that it may be due to faulty functioning of the endocrine glands.—P. J. Cammidge, Pr., Feb. 1920.

Diagnosis of cancer by serum reactions.—J. A. Shaw-Mackenzie, L. ii./22,759.

Cancer and some of its significant chemical reactions. There is evidence of increase of **Cholesterol** in the serum of carcinomatous patients and alteration in metabolism of fats and lipoids.—H. G. Reeves, L. ii./24,726.

The Lipase Theory.

It seems reasonable to conclude that the **diminution in lipolytic activity**, both in tumours and serum, is due to a real decrease in the production of esterases, though it is not suggested that these enzymes occupy

any very unique position in the problem of cancerous growth, beyond the excessive lipid-cholesterol ratio of tumours.—W. C. M. Lewis, B.M.J. ii./26, 923.

The main outcome of researches on Lipase since 1911 has been to show that natural and induced tissue *lipolysis with the fatty acids* or their Sodium salts are *important factors* in the protective processes and resistance of the body in malignant disease.—W. J. Simpson, B.M.J. ii./26, 1080.

It is difficult to avoid the suggestion that the labile chemical substance alluded to by Dr. Gye is of a similar nature to *inactive Lipase*, and that it can be activated by its own Chloroform-treated filtrate or co-enzyme. Dr. Gye notes that the agent or substance though sensitive to heat still retains its power in conjunction with the virus to produce a tumour. This brings the inactivated filtrate into line with the heated cancer extracts and filtrates with activating properties on pancreatic inactive Lipase.—J. A. Shaw Mackenzie, B.M.J. i./27, 78.

Criticism of Shaw-Mackenzie's views. Does not agree with view of hypercholesterolemia.—A. N. Currie, L. ii./24, 936. Reply, *ibid.* 1096.

Blood and tissue changes in cancer, with reference to diagnosis and treatment.—J. A. Shaw-Mackenzie, Jl. Trop. Med., Aug. 15, '25, 297. See also *ibid.*, Dec. 1, '27.

Cancer deemed a Constitutional disease.—Patients who have previously shown *signs of glycosuria later suffer from cancer*, or, in other words, glycosurics who have died have died of cancer. A case of true pancreatic diabetes never known to develop cancer. The metabolic error in glycosuria must be understood, to elucidate malignant disease. In glycosuria sugar appears in the urine in spite of its having been prepared for combustion by insulin, and the reason for its not being burnt is that its final oxidation is only achieved by the simultaneous oxidation of fat. It is obvious, therefore, that the fat cannot have been prepared for oxidation, and hence there must have been a *deficiency of Lipase*. Conversely, in pancreatic diabetes, the fat is ready for complete metabolism, but the sugar is not. The fats of the body, while acting as stores of potential energy are in other ways important cell constituents. They are part and parcel of cell protoplasm. Even in animals killed by starvation, when all the reserve fat is used up, the fats in the organs and tissues remain constant. This 'organised' fat, essential to life, is unsaturated and consists largely of phosphatides, in contradistinction to reserve fat, which is saturated, and it is important to note that whereas saturated fats are inactive, the more unsaturated they are, the more unstable they become.

The liver contains a relatively large amount of unsaturated fatty acids—in that organ, no doubt, the first stage of fat catabolism occurs. LEATHES and MEYER-WEDELL's rat experiments in 1923 proved that it is the function of the liver to prepare fats in this way, rendering the saturated acids unsaturated.

Neutral fat, when called upon for the needs of the organism, is taken direct to the liver, where it is converted largely into phosphatides, and the fatty acids unsaturated. The phosphoric compounds play an important part in the intermediary catabolism of carbohydrates. The fat is now ready in an unstable form for the repair and maintenance of tissues, in conjunction with carbohydrates which have been prepared by Insulin.

The unsaturated fats not only share in the cell structure, but also in the formation of the cell envelope. The pre-cancerous condition thought to be a *state of starvation of organised fat of the cells of the tissues, upsetting normal metabolism*. This deficiency lessens the power of cohesion in the protoplasmic particles, which is the most powerful obstacle to the operation of chemical affinity. Growth, which results from chemical changes in the cells of the tissues, will be accelerated in proportion to the increased rate of chemical change, and a tumour results, appearing first in those cells which by previous irritation and more rapid repair have also been exhausted of their fats, bringing about molecular disturbance and causing the protoplasmic molecules to become arranged in a random manner. The cell envelope, also consisting largely of phosphatides, becomes disorganised. Owing to this weakening, the protoplasm is allowed to sally forth, form irregular unions, and multiply illegitimately. Some of the nomadic cells are washed into the lymph stream and cause metastases, the defending cells being unable to resist them owing to a deficiency of organised

fat. It is not to be held that all people who have at some time had glycosuria develop cancer. There must be a previous irritation of the site where the tumour develops. This theory may explain cancerous cachexia, which resembles the cachexias of other metabolic diseases. Death does not always result directly from the cancer, but from exhaustion of the cells of the organism, due to a deficient supply of unsaturated fatty acid compounds.

It may also explain the difficulty of transplanting animal cancers from one species to another, as each species has a characteristic fat.

Occasional success with organic extracts, *e.g.*, thyroid, thought to be due to the Lipase-stimulating effect of these compounds.—J. T. Shirlaw, *Pr.*, Feb. 1929, 119-125.

Carcinoma of the Stomach—B.M.A. Discussion.

SIR W. I. DE C. WHEELER pointed out that 10,000 people died annually in the British Isles from this condition. X-ray examination was the best method of diagnosis—analysis of gastric contents and fractional test-meal of little value. Venous thrombosis a valuable sign of early carcinoma of the stomach. If there were no gain in weight, or maintenance, after medical treatment, malignant disease should be suspected and exploration was more than justified. E. I. SPRIGGS agreed as to the importance of X-ray examination, and gave an account of the clinical manifestations. A. F. HURST considered the presence of blood in every part of a fractional test-meal evidence of malignant disease, unless there had been recent hæmorrhage from an ulcer. Character of 'resting juice.' The stomach should be completely evacuated before the meal. The 'juice' often does not exceed 50 Cc. in normals. More than 50 Cc., and certainly more than 100 Cc., suggests presence of some difficulty in gastric evacuation. Test for starch. If free Hydrochloric Acid is present, an ulcer is probable cause. If there is no free acid, and especially if the material removed is uniformly thick, a growth is almost certainly present, especially if of foul odour and containing excess of organic acids. **Acidity:** In a consecutive series of 1,000 fractional test-meals complete achlorhydria was found in 15.2%. The presence of free Hydrochloric Acid cannot be regarded as evidence against the diagnosis of a growth. **Blood:** Constant presence of, in association with achlorhydria, only observed in cancer of the stomach. A skilled radiographer could show an abnormality of the stomach in 100% of cases of malignant disease. Occult blood was present in 100% cases and should always be examined for; it was never present in normal people.—L. ii./25,379; B.M.J. ii./25,379.

The determination of the serum bilirubin and the Phenoltetrachlorophthalein Test promise to be of assistance in the study of patients with abdominal carcinoma and suspected malignant disease of liver.—*per Pr.*, Feb. '26, 170.

Serum Diagnosis.

New Flocculation Reaction in malignant disease.—H. J. B. Fry, B.M.J. ii./25,4.

THE BOTELHO REACTION is based on the fact that with an acidified solution of Iodine, cancerous scrums give a permanent precipitate in the presence of definite quantities of the reagent; if physiological salt solution is added the results vary with the degree of dilution—a positive result obtaining with dilute serum, and a negative with concentrated serum; more definite results obtained by using serum with ascertained protein content (78 to 80%). TEDESCO-POLACK'S modification said to yield more definite and constant results, uniformity in the protein being secured by preliminary correction of the refractive index of the serum by means of the refractometer; the reaction is easy of manipulation and interpretation.—B.M.J. i./27,109. See also L. i./26,1157.

Theories as to Cause of Cancer, and Details as to Distribution, Increase, etc.

In 'Protists and Disease,' 1922, Jackson Clarke tells how in water-cultures of Molluscum Contagiosum the diagnostic corpuscles go through changes, which prove them to be parasitic protists, and he names the species *Plassomyxa contagiosa*, and the group to which they belong Plassomyxineæ. Comparative study showed them to be nearly related to *Synchytrium*, a genus of fungi parasitic in the epidermal cells of plants. In certain stages they are in the plasson state, *i.e.*, the same state as true nucleoli or karyosomes. At other stages they are nucleated; or, again, motile, as spironemes. In the Plassomyxineæ he includes the casual agents of smallpox, hydrophobia,

syphilis, and the common spontaneous human cancers and sarcomas. From X-ray and some other epitheliomas plasmomyxines are absent, and for such growths the term 'imitation-cancer' is used. This interpretation is opposed to that involved in the term 'cancer cell'; it is in harmony with results obtained by therapeutic doses of X-rays, radium, Coley's fluid, etc. *Lancet* reviewed the work.—L. ii./21,495.

Cancer thought to be caused by **anaerobic bacilli**—such organisms (rods) observed by direct examination of epitheliomata.—Ford Robertson, B.M.J. ii./21,199. See also W. McAdam Eccles, B.M.J. ii./21,199.

Relation of carcinoma to infection. Vaccines of anaerobic diphtheroid bacillus obtained from a breast cancer used. Tumour and ulcer diminished in size.—W. Ford Robertson, B.M.J. ii./21,929.

Cancer appears to be developed in precipitated **Glycogen** in the liver or other organ. As the Glycogen cannot be taken up by the normal cell tissue it is broken down and used by a dissipated sperm cell or species of yeast cell. It may be precipitated along with fibrin by a blow especially if situated near a vein. When a growth starts changes take place in composition of the bile salts, the patient becoming yellow or white in complexion. Cancer appears to be an asexual reproduction of the body.

Possible ovarian origin of carcinoma in women, at any rate of mammary cancer. Oophorectomy tried for inoperable mammary cancer with complete disappearance of the outward manifestations of cancer after the operation. Some form of pigment may be the actual exciting cause of cancer.—Sir G. T. Beaton, L. ii./22,655.

In cancer there is an infiltration of the waste products into the tissues—causing what is termed cachexia.—J. R. Huck, C.D., Oct. 16/20, Nov. 27/20, May 14/21, July 2/21.

Etiology. Statistics; tobacco, nervous temperaments.—B.M.J. i./22,964.

Cancer increasing in most countries. Striking data.—L. ii./21,347.

Cancer, its cause and cure.—Lord Athelstan and Sir W. Veno's Reward.—L. i./22,236.

Diet for providing foods deficient in **Fat Soluble A vitamin**—may possibly influence.—S. Monckton Copeman, L. i./22,966.

Education of the public advised through the daily press.—J. E. Adams, L. ii./22,639. See also Edwin L. Ash and S. Davies, *ibid.* 735.

Cancer theories. Many of them relative to food cannot be proved one way or the other, e.g. excessive tea drinking compared with the amounts taken by our ancestors. The **cold storage of food** could with advantage be investigated. The tissues of a carcass before freezing and after importation and the thawing process would be worth investigation. There would probably be a marked difference in values from the nutrition standpoint.—M.P.C. July 26th, 1922, p. 68.

A German surgeon made the proposal years ago that all women should have the uterus removed after the menopause. It would no doubt sensibly reduce the incidence and mortality of cancer. If we can identify the agencies which by continued action lead up to the *development* of cancer we can begin to build up a rational prophylaxis. It can only be a question of time until the active-cancer-producing constituent of tar is identified and tar-workers are protected.—Leader, L. ii./22,673.

Relation of Carcinoma to infection. Several cases of human carcinoma recorded in which definite local and general reactions occurred after inoculation with vaccine prepared from **diphtheroid bacillus**. Preparation of media, technique for inoculation and examination of media described.—W. M. Ford Robertson, L. ii./23,330.

A report on the **geographical distribution** of cancer mortality—results of a questionnaire sent out in 1923 by the Office International d'Hygiène Publique. There is almost unanimous belief that mortality from cancer is on the increase, Norway alone not subscribing to this belief.—L. i./24,352.

Incidence of cancer in Egypt—an analysis of 671 cases.—R. V. Dolbey and A. W. Moor, L. i./24,587.

The Natural duration of cancer. Statistics compiled from records of Middlesex Hospital over a period of 40 years. Two facts emerge: (1) the earlier the age of onset, the shorter the total duration of the untreated disease; (2) the natural duration of cancer at one and the same primary site is longer in the female than in the male.—W. S. Lazarus-Barlow, B.M.J. ii./24,266.

Increase of annual death-rate from cancer from 0.32 per 1,000 in 1860 to 1.21 in 1921. In this country the tendency is for deaths from cancer to occur later in life than formerly, with an excess of deaths of females over males, due entirely to malignant disease of the breast and generative organs. There is no evidence to show that it is infective or contagious, nor has it been proved that hereditary disposition is of practical importance, or that any particular article of food increases or decreases an individual's liability, or that any danger exists in inhabiting houses in which cancer happens to have been exceptionally common.

Cancer frequently follows prolonged irritation of certain tissues and prophylaxis consists in the removal of such sources of irritation as is possible. Early diagnosis is of great importance, and all cases of a suspicious nature, even such as the tendency of a wart or mole to grow should have immediate medical attention. The value of propaganda and facilities for diagnosis and treatment is emphasised.—MINISTRY OF HEALTH REPORT, Aug. 14/23.

The elucidation of cancer.—L. W. Sambon, *Jl. Trop. Med.*, June 2/24, 124.

The stomach is the seat of the disease in nearly 22% of the fatal cases in males in England and Wales. In females the generative and mammary organs are affected in more than $\frac{2}{3}$ of the total cases.—E. F. Bashford.

Chronic traumatic mastitis caused by CORSETS improperly made or worn. G. L. Cheatle.—*B.M.J. i./11*, 492.

Genesis of cancer. An enquiry showing cancer to be explainable as an essentially physiological tissue change not associated with any external cause, *e.g.*, parasite.—A. Turnbull, *B.M.J. ii./13*, 905

Cancer proteins exhibit a high content of Glutaminic Acid, Alanin, Phenylalanin and Aspartic Acids. The paper concludes in praise of 'X' ray or Radium irradiation, combined with saturating the part with Aniline Dyes.—W. J. Morton, *N.Y. Med. Jl.*, March 30th, 1912.

Two completely independent factors underlie the change of a normal cell into a cancer cell (1) an antecedent cell susceptibility, often acquired as a result of chronic irritation, (2) the cancerogenic factor (parasite). An organism with complex life story has been obtained almost constantly from cancer—it possesses yeast, coccal, bacillary and amorphous phases, each of which can grow true to type and live an absolutely independent life. Evidence obtained that the parasite lives in symbiosis with cancer cell in amorphous phase, and all other phases are derived from this during incubation of a cancerous growth; morphological features resemble life story for other classes of pathogenic organisms; belongs to familiar bacteria widespread in nature. The small proportion of men and animals developing cancer, in spite of the universal exposure, suggests all-importance of cell susceptibility and explains difficulty of producing cancer experimentally by injection of the organism.—James Young, *B.M.J. i./25*, 64.

The **Young-Glover** micro-organism (a pleomorphic micro-organism isolated simultaneously but independently by Young in Glasgow and Glover, in Toronto) is a microbe which, while possessing as alternative phases coccal, bacillary, yeast, and hyphal forms, lives ordinarily in the cancerous tissue as a dispersed element so minute as to be invisible. Loudon and McCormack (*Canada Lancet & Prac.*, Nov., '25) claim to have confirmed that this micro-organism is identical with the filterable virus of Gye and Barnard, and M. J. Scott (*Northwest Medicine*, Apl. and Oct., '25) claims to have isolated the Young-Glover microbe and to have produced malignant epithelial tumours in lower animals (monkeys) at the point of inoculation; he also claims to have cured a considerable number of cases (case reports of two are given) of cancer with a serum obtained from young horses immunised against an antigen prepared from the Young-Glover microbe.—James Young, *B.M.J. i./26*, 67.

Diet and Cancer.

A report to the Min. of Health by Monckton Copeman and Major Greenwood concerning an inquiry into the deaths from cancer in religious communities whose members live under strict dietary rules, involving more or less complete **abstinence from meat** and rich and abundant food shows that the incidence of fatal cancer, either in females or males, in such communities is **not lower** than that in the general population.—*B.M.J. i./27*, 153.

Filter-Passing Virus.—Criticism of Gye's Work.

W.E. GYE AND J. E. BARNARD showed that under certain conditions malignant new growths can be produced by **Filterable Viruses** and these have been photographed by means of a special microscope and ultra-violet light.—L. ii./25,109,135.

A review of work leading up to Gye and Barnard's researches.—L. ii./25,135. See also *ibid*, 302,408.

Discussion on filter-passing viruses and cancer.—B.M.J. ii./25,189-195.

GYE fails to state whether or not cultures derived from rat and mouse tumours will on addition of the specific factor produce likewise tumours in mice and rats, though such positive result is needed. It would be necessary not only to propagate the parasite but also to prepare a culture, and through inoculation from the culture to secure further cultures from which tumours are produced. Gye's results are impaired in that the so-called chicken sarcomas are usually regarded as different from the sarcomas of man and as merely infective granulomas; in any case they are biologically, of all animal tumours, the farthest removed from human cancer. Gye's results are of paramount importance for the role of a virus or a group of viruses in the pathology of tumours, though all his conclusions are not justified. As several workers have obtained 100% positive results in cancer formation by applying irritants, one cannot ascribe the inorganic production of cancer by tar, etc., to a parasite (the irritant causing tissue changes and preparing the way for infection by the virus, which then penetrates the cell and propagates), unless one arrives at the improbable conclusion that the virus is ubiquitous. It is possible however that the bacteria outside and inside the tumours are laden with a virus which is further cultivated with the propagation of the bacteria, and it is probable that other organisms may take up the virus, in which case various parasites might acquire carcinogenic properties. What Gye failed to accomplish—**production of cancer-like tumours in rats and mice with a virus derived from human cancer**—BLUMENTHAL did with his bacteria; the bacilli themselves were not demonstrated in the tumour, but were found in the droplets resulting from liquefaction of the tumour. It would be a further advance if it could be shown that the cancer-producing properties of these parasites were due to a virus or group of viruses, and although Gye and Barnard have not succeeded in this demonstration, their researches constitute an important step. Gye's discovery that the **virus has to be cultivated anaerobically** is of special interest and is in agreement with the findings of other workers, *i.e.*, that **cancer cells are anaerobic** in contradistinction to normal cells. Gye's experimental results are in harmony with the findings reached in other ways and although his researches do not furnish an unequivocal solution of the origin of cancer, they give a stimulus to research.—Prof. Blumenthal, D.M.W., per Jl. A.M.A. ii./26,625.

The virulence of a filtrate of chicken sarcoma can be increased or diminished by addition of a variable quantity of an acid salt, the **mono-potassium phosphate**. Gye neglected this factor, never having controlled it, but each time he was able to show activation or virus acidity was added, whilst non-active control injections were always in neutral or slightly alkaline solutions. Neither his two factors, nor his supposed "cultures" of the virus of neoplasma, necessary or proven.—E. Harde, Jl. Trop. Med., June 1, '26, 159-161.

Gye's work leads to the conclusion that the entrance into a normal cell of a specific virus confers on the cell characteristics which are the essential features of malignancy; this virus is apparently the same for many different classes of animals; alone it is unable to effect entrance into a normal cell, but requires an accessory biological factor—in the case of the ROUS TUMOURS a chemical substance furnished by the tumour cells; it is not essential that the cells of every neoplasm must produce such a substance—it is sufficient for the virus to be able to enter a few cells. The cells of the ROUS TUMOUR are exceptional in forming an abundance of this specific factor; further work will have to show whether different sarcomata vary in the amount of stability of the specific factor formed by them. **The virus by itself is non-pathogenic, which explains why the disease is non-contagious.** Gye's work has solved our old and fundamental difficulties—it does not compete with any previously established facts, but confirms them; it is the first adequate explanation of the causation and growth of cancer.—W. Cramer, B.M.J. i./26,175-180.

Effects of antiseptics on Rous tumour extracts. Chloroform, Phenol, Sublimate, Toluene, Ether, Hydrogen Peroxide, Formalin, Acriflavine, and Hydrocyanic Acid have been tested and found effective in abolishing the activity of the extracts. Chloroform acts very rapidly, Acriflavine slowly. There is, however, an agent contained in tumours of diverse origin and of diverse structure which can reactivate an extract which has been inactivated by an antiseptic. The agent is a living filtrable microbe and is the cause of new growths.—W. E. Gye, B.M.J. ii./26,865, see also *ibid.* 897.

Experiments confirming the presence in Rous sarcoma fluid of two casual factors which, individually inert, in combination give rise to tumour growth. In other points digressing from Gye's work.—R. D. Mackenzie and C. F. W. Illingworth, L. ii./26,745.

Irritants in relation to Cancer.

Arsenic Cancer.—Arsenic may well be one of many predisposing causes. A case described of a woman who had psoriasis treated by arsenic and who ultimately died of cancer, also a table of numerous allied cases.—L. ii./13,210,284. See also Sir J. Bland Sutton, B.M.J. ii./16,788.

Tar cancer experiments on mice.—J. A. Murray, B.M.J. ii./21,200,795.

Imperial Cancer Research Fund—Seventh Scientific Report. Production of squamous-celled carcinoma in mice by Tar.—B.M.J. ii./21,910.

An investigation into the presence of **copper** in tumours and normal tissue, carried out in great detail, showed its presence in over 100 specimens with only one exception. Practically all the internal organs were examined and considerably increased amounts of copper were found in degenerated tissues, as much as 501 mgm. per kilo being present in a carcinoma of the rectum. Suggested that this increase shows that degeneration is associated with an increased catalytic action due to increased amount of copper, or that Copper, like Calcium, tends to be deposited in degenerated areas.—C. P. White, L. ii./21,701.

Local irritants causing Cancer. Details of the causation of epithelioma by the carrying of the kangri, a portable fire basket, by natives of Kashmir; also details of pitch cancer, or fuel workers' cancer.—B.M.J. ii./10,629; i./11,885. See also L. ii./10,1830

Chemical irritants, Sulphurous and Sulphuric Acid, also Tar have been held responsible for cancer.

Sulphur content in fuel in relation to cancer. Peat is found in parts to be stronger in Sulphur than others and it appears cancer mortality is connected with high Sulphur content.—L. ii./13,506.

Gasworks Pitch and Cancer.—Men handling pitch or engaged in making briquettes occasionally suffer from warty growths which may ulcerate and become the seat of epitheliomatous cancer, or particles of pitch strike the eyes and induce severe inflammation of the conjunctiva and cornea which may end in loss of vision.—B.M.J., i./13,36.

Briquettes and the incidence of cancer. The mischievous ingredient is an Amidine which distils at about the same temperature as Anthracene Oil, and is present in the rough Anthracene cake.—B.M.J. ii./13,506.

Liquid Paraffin is harmless and not likely to have any of the evils of pitch and tar in the cause of pitch cancer.—H. C. Ross and J. W. Cropper, B.M.J. ii./13,48. It is one of the later products of distillation of crude petroleum and is therefore probably quite free from "Auxetics" which have been found in the "interim Oil Scales" produced at oil works in Scotland.—B.M.J. i./15,445,530.

190 Mice painted with Coal Tar once or twice a week. 23 developed *true* cancer of the area painted.—L. ii./21,1117.

Prof. B. Bloch, of Zurich, has succeeded in locating the cancer-producing agent of Coal Tar in the fraction with b.pt. over 300°C. It is soluble in Benzol. 100% of mice to which it was applied gave rapidly growing carcinomata within 4 months. The hydrocarbons with lower b.pt. also produced tumours, but these were benign. It was found that while tumours could be produced in rabbits and mice by applying tar, guinea pigs so far failed to react. This emphasises the susceptibility of the cell as an important factor in genesis of cancer.—L. ii./21,1235.

Tar applied to mice for a time and the irritant then removed; tumours and even carcinomata may appear later.—A. Leitch, B.M.J. ii./22,1101, see also J. A. Murray, *ibid.* 1103.

Paraffin Cancer and its experimental production. By analogy with these results on mice it takes at least 10 years of exposure to paraffin oils to produce cancer in man—agreeing with actual experience.—A. Leitch, B.M.J. ii./22, 1104. See also Soot Cancer, *ibid.*, p. 1113 and Arsenic Cancer, p. *ibid.*, 1107. The theory of irritation hence becomes more impressive.—*ibid.* 1130.

Condemnation of soaps, face powders, creams, bath salts, as being conducive to cancer through irritation of the skin.—Sir G. Lenthal Cheatele, P.J. i./23, 347.

"Occupation dermatoses" occur in approximately 50% of the workers engaged in refining Paraffin in the Scottish Shale Oil Industry. Types of dermatoses described. The lesions appear soon after the commencement of work in the Paraffin departments and persist throughout the length of employment as Paraffin workers.—Report of Imperial Cancer Research Fund, L. ii./23, 1370.

The cancer incidence among Paraffin workers in the Scottish Shale Oil Industry is 0.1% per annum. The condition occurs in workmen about, or over, middle life, who have been Paraffin workers for long periods—20 years or more.—Report of Imperial Cancer Research Fund, L. ii./23, 1371.

Cause of Cancer—an experimental inquiry. Description of Fibiger's work on gastric cancer in rats (cockroach experiments). Fibiger was the pioneer in the experimental inquiry into the etiology of cancer. *Cysticercus sarcoma* (due to *C. fasciolaris*, the larval stage of *tænia crassicolis*, afflicting rats) found in the liver of rats, occurring round the parasitic cysts. It is often said that cancer is a disease of old age, but this is by no means the case.

Tar Cancer. There are grounds for believing that in human cancer, the antecedents of which are, for the present, hid from us, some irritant may have been in action and have disappeared, leaving no evidence of its presence, long before the cancer declared itself. Remarkable differences in toxic action and tumour-producing powers of tars. Some experiments of Murray suggest that the occurrence of one form of cancer in an individual protects the body in some way against the occurrence of another (further work needed). Some day it may be possible to isolate endogenous carcinogenic substances, local malproducts of metabolism, it may be, which have similar effects on tissues as the irritants dealt with. A future generation, knowing surely the causes of cancer, will have no patience with the present-day floundering, the guesses, and the contending arguments. Age in itself is not an important factor. It is a question as to the time the causal agent has been in operation. If we expose a child of 10 and an adult of 40 to the same carcinogenic agent and the latent period necessary is 10 years, the cancer would declare itself at 20 in the former and at 50 in the latter.—A. Leitch, Director of Cancer Hospital Research Institute, London, B.M.J. ii./23, 1. See also L. ii./23, 1369.

The cancer-producing factor in Tar. Industrial evidence alone shows that the cancer-producing substance is present in the higher boiling fractions of tar, creosote oil, anthracene oil (and hence in green oil and anthracene) and pitch. Experimental evidence further shows that the substance is not concentrated in the solids suspended in anthracene oil and that it is present in the highest boiling distillate obtainable from pitch. Hence it may distil over through an interval of temperature from 250° C. (the creosote fraction) to over 500° C. (the "pitch distillate")—a range of 250° or more. Attempts to find the cancer-producing substance among the known constituents of coal tar have so far given negative results. It seems not unlikely that the substance is a compound, unstable, and present in amounts as small perhaps as those of the vitamins in food.—E. L. Kennaway, B.M.J. i./24, 564.

Nine products tested re production of cancer after heating them to temperatures stated (1) Acetylene 700° C.; (2) Acetylene 800—900°; (3) Californian Petroleum 880°; (4) Isoprene 700°; (5) (6) and (7) Durham Holmside Coal 450°, 560° and 1,250°; (8) Human Skin 920°; (9) Yeast 920°. The tarry products were applied twice weekly to mice (generally 100 for each test) in the interscapular region. It is not correct to call these pyrogenous materials cancer producers simply because they are irritants. The irritation must be of a special kind, or must act on some special elements in the tissues. Cancer was produced by the above procedure by substances obtained by heating **Acetylene, Isoprene, Yeast and human skin to temperatures ranging from 700 to 920°**. Acetylene is the simplest organic compound from which a coccigenic material has been so far obtained. The Californian Petroleum which produced no tumours of any kind in mice,

in the unheated state, showed active cancer-producing properties after exposure to temperature of 880°. The cancer-producing substance present in Coal Tar is found in small amount below 450°, at 560° it appears in larger quantity, and this increase continues at a slower rate up to 1,250°.—E. L. Kennaway, B.M.J. ii./25,1.

Behaviour of Coal Tar in the tissues.—L.H. Jorstad, Jl. of Cancer Res., per Jl. A.M.A. ii./25,852.

Cancer of the **scrotum** is sufficiently common among a certain class of cotton-spinners as to be known as '**mule-spinner's disease**.' Said to be due to the scrotum coming in contact with a part of the machine, coated with lubricating oil, which impregnates the spinner's pants.—B.M.J. i./24,679. It also occurs among sweeps, tar and paraffin workers.—A. H. Southam and S. R. Wilson, B.M.J. ii./22,971.

On July 26th, 1924, at Ashton-under-Lyne, judgment was given in favour of a cotton-spinner, who claimed damages under the Workmen's Compensation Act for cancer of the **scrotum** ("mule-spinner's disease") contracted as a result of his employment (irritant action of mineral oils specifically mentioned), the Judge remarking that "the conclusion is irresistible that there is a connection between the disease and the employment."—B.M.J. ii./24,287.

Mule-spinners' cancer and Mineral Oils, and a note on Chimney-sweepers' cancer.—A. Leitch, B.M.J. ii./24,941.

Importance of early diagnosis in mule-spinners' disease, when operation is simple and gives lasting cure. Surgery the safest and most satisfactory method.—A. H. Southam, B.M.J. ii./28,438.

Betel-chewing and cancer.—B.M.J. ii./23,632,680,733.

Though Betel-nut chewers in India have been proved to suffer from buccal cancer as a result of the habit, the disease in Formosa is comparatively rare though the natives are equally addicted to Betel-chewing. Can this be attributable to a racial immunity or to an unknown factor operative in India and not in China?—B.M.J. i./24,729.

Cancer is as much one of the results of **chronic intestinal stasis** as appendicitis, colitis, etc. Cancer never attacks a healthy organ or tissue, and the most common cause of the degenerative changes in the structures of the body is chronic intestinal stasis.—Sir W. Arbuthnot Lane, Pr., April 24/205. See also B.M.J. ii./23,745.

Death Rate. Statistics on Epidemiology.

The death rate in 1926 was 1,362, as compared with 1,336 in 1925. This does not indicate an actual rise as explained in Vol. I., p. 1043.

From statistics based on 2,000 cases (1900-1924) at the Cancer Hospital, S. Wyard concludes that no confirmation is given to the views of Lazarus Barlow, and that the duration of life appears fairly even throughout all the age periods. Neither do the statistics indicate that the duration of life is greater in females than in males.—B.M.J. i./25,206-7.

'The transference of cancer from one individual to another must be rather rare, if taking place at all,' and cancer certainly does not show a marked preference for certain families.—J. Thoner, from continued observations in Norway, L. i./25,399.

The statistical association of cancer mortality and goitre.—P. Stocks, B.M.J. i./25,84.

From experiments and observations, it appears that a **predisposition to cancer may be transmissible by heredity**.—P. Lockhart-Mummery, L. i./25,427.

Cancer of the breast.—The normal duration of unoperated cases (from onset to death) averages three years, and that of operated cases averages 5 years.—S. Wyard, L. i./25,1181.

Researches on the epidemiology of Cancer in Iceland and Italy.—L. W. Sambon, Jl. Trop. Med., Feb. 2, '25, 39-71.

It is only in relatively early cases, where the primary growth does not involve a vital area, or in advanced inoperable cases, that destruction and absorption of cancer or sarcoma may be followed by restoration to good health.—J. G. Adami, B.M.J. ii./25,978.

Cancer mortality in U.S.A.

Pronounced **increase in death-rate** from cancer in persons 40 years and over in the ten original registration States, *i.e.*, Connecticut, Indiana, Maine, Massachusetts, Michigan, New Hampshire, New York, Rhode Island, and Vermont, 30% of which is due to greater accuracy in filling up of death

returns, the remainder being an actual increase, resulting in a death rate from 25 to 30% higher than it was 21 years ago.—J. W. Schreschewsky, *Jl. A.M.A.*, ii./25,1179; see also *ibid.* 1505.

Half-a-million people die of cancer every year, of which Europe is responsible for 300,000 and N. America for 95,000. England's figure is 45,000, France 24,000, Italy 27,000, and Argentina 5,696. No race or climate exempt, but women develop cancer at earlier age than men per *Jl. A.M.A.* ii./25,1263.

In regard to the bowel, pancreas and prostate, cancer is relatively more common in people of high social status. There is a relation between the soil and the frequency of cancer.—*P.J.*, i./26,293.

Special cancer number. Observations and researches on the epidemiology of cancer made in Holland and Italy (May-September, '25).—L. W. Sambon, *Jl. Trop. Med.*, Aug. 16, '26,233-287.

The analysis of data supplied by monastic communities proves conclusively that fatal cancer occurs in populations abstaining from flesh food.—Min. of Health Report, No. 36, Diet and Cancer, L. i./27,202.

A 50% reduction in mortality from cancer of the breast and uterus could be achieved with present methods if all women would attend for radical operation at an early stage of the disease. At present the condition of little more than half the applicants is operable. Confirmed statistically on calculations based on survivals among known cases.—L. i./27,303.

The Natural Duration of Cancer.

From an analysis of 4,238 cases, Major Greenwood (Reports on Public Health and Medical Subjects, No. 33, Ministry of Health, 1926) states that the mean duration in months for seven primary sites was found to be 38.3, 20.9, 26.7, 16.5, 12.0, 14.5, and 16.8 respectively in cancer of the breast, uterus, rectum, tongue and mouth, œsophagus, larynx, and stomach. There seems to be little relation between the age of onset and the duration. A **Survivorship Table** has been constructed calculating the chances of survival from 0 to 6 years after the onset of cancer in each region in untreated cases. For cancer of the breast the normal expectation of life of a woman of 55 is 18.87 years, that of a woman with untreated cancer of the breast is 3.25 years; that of one operated on under 'average' conditions is 5.74 years, and of one operated on under the best conditions 12.93 years. Resort to early operation for cancer of the breast would add thousands of years to the active life of the nation.—L. ii./26,188.

Treatment.

Cancer Antiserum.

By repeated injection of finely divided mouse carcinoma into a rat or rabbit a concentration of antibodies can be obtained in the serum which will kill cancer cells in vitro. Experiments on rats showed that the antiserum is definitely toxic and irritant, gives some cures in inoculated tumour and confers immunity. It is suggested that it might be possible to use an antiserum to prevent recurrence of tumour after incomplete surgical removal. T. Lumsden, L. i./25,383 and L. ii./25,539.

The ætiology of cancer in India. Cases of inoperable cancer are more frequent than in many other countries and the mortality from them is high. A treatment described consists of intravenous or intramuscular injection, together with local injections into the tumour, of *Ethyl Margosate and Copper*. This is followed in 24-48 hours by irradiation.—K. K. Chatterji, I.M.G., Aug. '26.

Sodium Oleate.—Good results obtained by combined treatment with intravenous injections of 2 Cc. 2% Sodium Oleate (warmed previously to 30° C.), and oral administration of a *Titanium-Lipase* compound, obtained by the action of a 10% solution of Titanium Tetrachloride on an aqueous solution of Lipase prepared by the Willstaetter method. In addition, in external eczema, treat with Titanium Ointment.—D. Gardner, *Jl. Trop. Med.* Aug. 1/28,195.

Colloidal Lead.

Two cases well treated in private practice—carcinoma of the breast and carcinoma of the rectum. Appreciable improvement following courses of intramuscular injections—12 Cc. at weekly intervals, with small injections locally into the nodules, a total of 12 grains of Lead being given in one case and 10 grains in the other. No acute toxic symptoms. The treatment does

not appear to merit such wholesale condemnation and adverse criticism as it has received.—E. Talbot, B.M.J. ii./28,1035.

The combined action of Colloidal Lead and radiation caused disappearance of tumours (experimentally) in doses which, by themselves, only result in temporary retardation.—J. C. Mottram, B.M.J. i./28,132.

Chemotherapy in malignant disease.—W. Blair Bell, L. ii./28,164.

Correct liver function necessary. Extent and interval of dosage dependent on existing damage.—L. Cunningham and M. M. Datnow, L. ii./29,655.

Lead Selenium Compounds.—Suspension of Lead Selenide in a gum ghatti solution of strength Lead (metal) 0.4% and Selenium 0.04% used in cancer, and a substance named D.S., the composition of which is not stated.—A. L. Taylor and E. Lloyd, P.J. ii./28,542.

Colloidal Lead Phosphate and Tetra-Ethyl Lead appear to be the only Lead compounds suitable for use intravenously in cancer. Tetra-Ethyl Lead emulsion is prepared by shaking 1.6 Gm. commercial Tetra-Ethyl Lead with a mixture made up of 150 Cc. water, 25 Cc. saturated Lecithin suspension and 10 Cc. 1% Sodium Oleate solution. Prepare freshly and shake vigorously before use. F. Bischoff and others, Jl. Pharm. & Exp. Therap., Sept., '28,109.

New Method of Administering Heavy Metals.—The patient's blood was drawn off into sodium citrate solution, the corpuscles were centrifugalised washed, combined with the metal, washed twice or three times until the supernatant fluid was free of metal, and then reintroduced intravenously in a saline suspension. Animal experiments showed that it was possible to administer intravenously in this way lead, copper, mercury, and other metals three to five times as great as would kill the animal if they were introduced intravenously in ordinary solution. The phenomenon is probably a surface effect of the nature of adsorption, or a specific combination of the metal with some constituent of the envelope of the corpuscle.—J. L. Jona, L. ii./28,15.

Fluorescein.

Good results in cancer with 2 to 5% solution of the Sodium salt painted **externally**, or **administered internally**, in a dose of 30 grains of the powder. Intravenous injections unnecessary owing to its extreme diffusibility. The external application causes no pain, and there are no unpleasant symptoms from the internal use, except yellow colouration of the skin, which disappears.—S. Monckton Copeman, B.M.J. ii./28,223.

Activated Fluorescein. Irradiation with 'X'-rays after local and/or internal use.—S. M. Copeman, Frank Coke, and C. Gouldesbrough, B.M.J. ii./29,233. A criticism.—J. H. Douglas Webster, B.M.J. ii./29,367.

Cancer control by Blood Alkalinity.

The cancer cell is simply an ordinary body cell compelled to live in the wrong liquid environment, due to excess of alkali with low content of Calcium. Irradiation treatment is successful in so far as it **reduces alkalinity of blood**. People suffering from **acidosis are practically immune from cancer**. There is a possibility of a family tendency to run low in body acid and high in alkali, and this tendency may be passed on. When a body cell finds itself in an abnormally alkaline environment it acts like a yeast cell; its walls expand and become more permeable; it divides, and increases in number and mass occur; as with Yeast, the addition of acid stops this growth. Probably it is not sufficient merely to administer doses of acid to a cancer patient, but necessary to attack chemically the course of alkali, or to **foster acid production**.—E. McDonald (Chairman of Cancer Research, Univ. of Pennsylvania), Am. Jl. Pharm., Sept., '28,607.

Uric Acid free diet in inoperable cancer. Results of trials of a diet of nuts, fruit, biscuits, etc.—A. Haig, B.M.J. ii./12,81,150.

Coley's Fluid.

Is prepared by cultivating the *Streptococcus* of erysipelas in bouillon ten days. *B. prodigiosus* is added, and the two are grown together for ten days. The culture is then killed at 60° C. *B. prodigiosus* has a curative effect on tumours, and intensifies the virulence of the toxins of erysipelas.

The method was founded on the occurrence of retrogression in, and disappearance of, inoperable sarcomata as a sequel to attacks of erysipelas. Six weeks to three months treatment generally sufficient.

The **Lister Institute** supplies Coley's Fluid (of red colour) in phials of 2 Cc. **Dose.**— $\frac{1}{2}$ minim at first, injected into the tumour, or $\frac{1}{2}$ minim if

injected elsewhere, diluted with sterile Distilled Water, gradually increased, e.g., by $\frac{1}{4}$ or $\frac{1}{2}$ minim daily, until a temperature of 102° to 104° F. is produced.

1 Cc. contains 600 millions *Streptococci*, 0.25% *B. prodigiosus* protein and 13.3% Glycerin.

Coley pointed out the necessity of following up this small dose by alternate local and *systemic* injections, also injections must be given until all reaction has calmed down and the temperature fallen.

Mixed-cell sarcoma treated locally, excision and Coley's Fluid $\frac{1}{4}$ to 3 minim doses, successful.—B.M.J. ii./13,1484.

For further methods of treatment of cancer including the Lead treatment consult the *Therapeutic Index*—Vol. I. p. 1042.

Cerebro-Spinal Fever.

For a detailed account of characters, types of the *Meningococcus*, *Bacteriology and Diagnosis* (West's Swab, Cambridge Hospital Medium, Congo Red Blood Serum), *Treatment and Disinfection of Carriers*, *Lister Antimeningococcic Serum*, *Flexner's Serum and Vaccine*, see Vol. I., p. 909 et seq.

Meningococci may be occasionally found in peripheral blood films by using Giemsa's stain.—A. C. Coles, L. i./15,750, 828, 1046.

C.S. fever treated by univalent serum intrathecally (20 Cc.).—H. S. Banks, L. i./20,591.

The meningococcus is a very slightly pathogenic organism, but its feeble virulence is largely counterbalanced by its remarkable power of multiplying. The susceptibility, the lack of resistance of the organism, however—not its movement towards the meninges—constitute the real reason why the general blood infection is as a rule of very short duration. As soon as the patient develops even the very slightest degree of immunity the meningococci present in the circulation are impaired in vitality, lose the power to bring about metabolic lesions, and finally are completely destroyed.—Ksawery Lewkowicz, L. ii./24,488.

Trypagar as a medium for culture of the meningococcus. Contains pea flour extract and Trypsin broth as follows:—

(1) Pea Flour Extract.

Mix Peaflour 100 Gm., Salt 100 Gm. with a litre of Distilled Water. Steam for $\frac{1}{2}$ hour with occasional stirring. Allow to settle and filter. Make fresh for each batch of Trypagar.

(2) Trypsin Broth (Douglas).

To each $\frac{1}{2}$ kilo of fresh bullocks' hearts freed from fat and vessels and minced fine add 1 litre of water and make faintly alkaline to litmus with 2% Potassium Hydroxide solution. Heat slowly to 75° or 80° C. 5 minutes. Cool to 37° C. and add 1% of Liq. Trypsin Co. and keep at 37° C. for $2\frac{1}{2}$ to 3 hours. Test for adequate peptonisation with Biuret reaction as below. Then render slightly acid with Glacial Acetic Acid and bring slowly to boil for $\frac{1}{2}$ hour. Leave over night in a cool place and decant the clear liquid. Make faintly alkaline to litmus and sterilise in autoclave at 118° C. 1 hour on each of two days.

To Make Trypagar.

Add 2% of Agar to Trypsinised Broth made as above and 0.125 Gm. Calcium Chloride per litre. Autoclave at 118° C. for $\frac{1}{2}$ hour to dissolve. Titrate a small quantity after well mixing, with N/10 Potassium Hydroxide while boiling (Phenolphthalein) and add KOH *q.s.* to the bulk to make *neutral*. Cool to 60° C., add white of egg with shells (two to the litre) and autoclave again at 118° C. for 75 minutes or in the steamer for 2 hours. Filter and add 5% Sterile Pea Flour Extract above and sterilise in the ordinary way.

The agar is directed to be cut up and washed with Dilute Acetic Acid (2.5 Cc. of Glacial per litre of water) and again washed thoroughly before use.

Sterile Blood Serum is directed to be added to the Trypagar in the proportion of 2% for use in primary cultures at the time of cultivation.

Biuret Reaction.

To 5 Cc. of broth add 0.1 Cc. 5% Copper Sulphate Solution, mix and add 5 Cc. N/1 Sodium Hydroxide. A true pink shows adequate trypsinisation. Bluish purple is incomplete.—Lieut. Col. Gordon, Maj. T. G. M. Hine, Capt. M. Flack, B.M.J. ii./16,678.

Chemical factors involved in growth of the meningococcus. The organism needs vitamins as in Gordon's Peaflour Extract for its primary growth *in vitro*, but during the early stages of subculture this need becomes greatly diminished. After a certain number of subcultures the organism will grow vigorously on a vitamin-free medium, providing there is an abundant supply of free amino acid. The tryptic digest of Casein (Cole & Onslow) fills these two conditions.—R.M.J. i./17,11.

Lange's Colloidal Gold reaction (1912) (*q.v.*) has been criticised as regard its validity as a test in diagnosis of neuro-syphilis. It was found that a positive gold reaction in cerebro-spinal fever is definite evidence of organic nervous disease.—C. Worster-Drought and co-workers, L. ii./22,1063.

Epidemiology of cerebro-spinal fever.

From 1914 to 1918, 6,450 cases were notified in England and Wales, the stress falling on urban dwellers during the winter and spring months, the usual incubation period being 1—7 days, average 4 days.—A. S. MacNalty, L. i./25, 532.

Mutability of Organisms. The meningococcus and other bacteria—data supporting.—B.M.J. ii./16,604.

Lord Lister, it may be mentioned, remarked 'it is far from impossible that there may exist ultra-microscopic organisms, as real, as distinct in structure and as potent in their effects as is the *Bacterium lactis*.' He saw, as in a glass darkly, the phenomenon, now familiarly described as those of 'sporting' or 'mutation' in bacteria, and clearly discerned that ultra-visible particles might play a part in these.—Sir W. Hamer, L. i./23,1009.

Transmutation of bacteria.—S. Gurney-Dixon reviewed, L. i./20,327.

Mutation of species. Higher organisms, protozoa, bacteria.—W. R. Brierley, B.M.J. ii./22,722.

There is now strong evidence to support the view that a similar morphological variability is common to all bacteria and that bacterial classification is in need of revision—'the very foundations of bacterial classification are tottering!'—James Young, B.M.J. i./25,62, 64.

Bacillus Coli Communis. A normal inhabitant of the intestines, but becomes virulent in certain conditions. It increases the virulence of typhoid. The *Bacillus Coli* is present in an infant a few hours after birth.

Could not be found in London air. Desiccation necessary for it to gain access to the air, which is generally fatal to this organism.—Hewlett.

BACILLURIA occurs with great frequency. 1. Associated with passage of pus; single abscess or more widespread infection of the urinary tract. 2. Milder stage—continuous passage of the bacilli but without pus or epithelial cells. 3. Intermittent passage of the bacilli. One often finds a history of constipation and a large proportion of cases are women.

In examining such urine in which pus is absent note (a) Pale colour, paler than one would expect from the gravity. (b) Low acid reaction; rarely very acid. (c) The urine is hazy, not clear. Filter a little, if still cloudy, examine under the microscope: ($\frac{1}{2}$ inch oil immersion). Round bodies or short rods (the former are the bacilli 'on end'). Note motility. Stain centrifuged deposit by Gram's method. It is Gram negative. The urine should be fresh and collected in sterile flask by catheter if possible. Inoculate an agar tube with a large loop full—note opaque white growth after 24 hours with crenated margin, also on Reibelagar or Conradi Drigalski medium.

Variability in the Gas-forming power of Intestinal Bacteria. It is possible to select a strain of *B. Coli* which fails to produce gas from certain Mono, Di-, and Poly-Saccharides.

The varieties of *B. Coli* are almost infinite.—L. ii./13,1241.

The typical characters of *B. Coli Communis* are as follows:—

Gram negative bacillus, producing acid and gas in Glucose and Lactose broths, acid and clot in milk, indol in Peptone-water, and fluorescence in Neutral Red. For further characteristics see *B. Typhosus* and Bacteriological Examination of Water, this volume.

Alternative modes by which *B. Coli* may bring about anaerobic decomposition of Dextrose.—B.C.A., '28, A1159.

Abnormal putrefaction in the intestine.—The presence of anaerobic bacteria is believed to account for this—normally the bacteria are either aerobic or facultative anaerobes mainly, whilst the anaerobic are in the minority. Excess of the anaerobic bacteria may be caused by excess

of animal food,—auto-intoxication can undoubtedly be traced to this. Against the food may be excessively contaminated with bacteria, *e.g.*, in pyorrhœa alveolaris, and post nasal catarrh. Further, it may pass from the stomach imperfectly digested. There is in addition purely intestinal putrefaction. One of the agencies of defence by nature against such injury is the combating of toxins by the intestinal flora—principally *B. Coli*—this organism is furthermore stated to produce thermolabile and thermostable substances which not only inhibit the growth of other organisms, but also their own if given long enough time to act.

Diagnosis of abnormal putrefaction may be assisted by estimating (1) URINE, increase in ethereal sulphates in the urine; increase in total output of aromatic bodies; rise in capillary constant; examination for Indican and other constituents. (2) EXAMINATION OF THE FÆCES,—staining by Gram's method and counterstaining with neutral red—the red organisms should preponderate. In abnormal putrefaction in proportion as the aerobic bacilli are replaced by strict anaerobes (mostly + Gram) the blue stained will be in excess. A loopful of a 1 in 100 suspension of fæces in sterile milk should not produce a rapid gas formation (*e.g.*, by *B. Aerogenes Capsulatus*).

Bacilluria and Pyuria.—Estimate the Acid Index by titrating 10 Cc. of the urine with N/10 Sodium Hydrate using Phenolphthalein. If low, administer Acid Sodium Phosphate thrice daily in order to increase the acidity up to even 10° and to keep it up. Albumin (due to Globulin probably due to Leucocytes) may be found, also Acetone.

The chief bacteria concerned are *B. Coli*, *Streptococci* of the long type, which are more feebly Gram + than *St. Pyogenes*, *Staphylococcal forms*, and "Beaded" bacilli of the *B. Xerosis* type, further a great variety resembling *B. proteus vulgaris*. All of these have been found in bacilluria with joint troubles, but the most striking cases afforded almost pure culture of streptococcal form. They closely resemble the *streptococcus salivarius*, a common inhabitant of the throat. Tubercle bacilli should always be looked for, especially if lymphocytes are present. Pneumococci are said to occur, but in connection with acute cases, while gonococci play an important role by themselves.

For the effect of Formaldehyde upon this organism (*i.e.*, on treatment with Hexamine and Sodium Acid Phosphate), see Hexamine this Vol., and recent data, Vol. I., p. 450,451.

B. COLI IN THE BLOOD.—Blood cultures made from persons suffering from undoubted Coli infections are almost invariably sterile. On three occasions pure growths of the bacillus were obtained from the blood. In two cases they were obtained whilst patients were actually suffering from a rigor and in the third 3½ hours after a rigor.—L. ii./12,1500.

Tuberculosis, rheumatism and many other chronic diseases thought to be the effect of the toxins which pervade the tissues as a result of absorption from the intestine in chronic intestinal stasis. Far reaching results are being achieved by the treatment of tuberculosis with detoxicated *B. coli* and other organisms.—White Robertson quoted by A. C. Jordan, L. i./20,760.

Infection of the blood stream by *B. coli* relatively uncommon. The chief portals of entry in order of frequency are the urinary tract, the female genital tract, and the intestinal tract. *B. coli sepsis* occurs more frequently in women from 20 to 40 and in men from 40 to 70.—Jl.A.M.A., May 3, '24; Jl. Trop. Med., July 1/24,195.

For **Musgrave's Medium** for cultivating *B. Coli*, see Culture Media.

For *Distinction and Separation from B. Typhosus* vide Bact. Examination of Water and *B. Typhosus*.

Dhobie's Itch.—Manson states many cases are produced by *Microsporon minutissimum* and are really inflamed erythrasma and not trichophyton ringworm.

Bacillus Diphtheriæ.

Directions for collecting specimens.—If a sterile swab is not at hand (which should be used with aid of a tongue depressor), a small piece of absorbent cotton wool (not medicated with an antiseptic) should be steamed, *e.g.*, at the mouth of a kettle, allowed to cool and rubbed over the membrane on the fauces of the patient and removed in a test tube or bottle which has been similarly sterilised. If possible a small portion of the membrane should be

detached in addition. The organism may persist for many months in nasal and aural discharges also in dry condition. an important point to recollect in disinfection of bed linen. Moist heat destroys the organism rapidly, *e.g.*, a temperature of 60° C. Is also very sensitive to treatment by antiseptics. Nurses in charge of patients should be examined occasionally as the organism may be present without symptoms of illness and infection by such agency should be guarded against. An injection of Antitoxin is a safeguard, or in preference Toxin-Antitoxin *q.v.*

Films are prepared from the swab. Stain by Gram's method (Gram +) also by Pugh's or Neisser's Stains to show metachromatic granules. Dry and mount in xylol balsam.

Recognition.—*B. diphtheriae* may be distinguished from the other organisms which will probably be seen in large numbers by the following characteristics:—Irregularity in size and outline straight or slightly curved, more or less clubbed at one or both ends (clubs chiefly in cultures), sometimes spindle shaped, or as curved wedges, occasionally irregularly segmented, rarely or never regular in outline. Parallel grouping and 'Chinese alphabet' characteristic. Stain irregularly. Show irregular beading and metachromatism. Cultivate on Loeffler's blood-serum—fine cream-coloured growth in 12 to 16 hours, and the film from this stain with methylene blue, Neisser's or Gram's method. Cultivations should in all cases be made on blood-serum or glycerin agar before the result of diagnosis can be positive. Further characteristics,—no spores, non-motile. Form differs with culture medium.

Neisser's method of staining the organism:—

Stain $\frac{1}{2}$ minute each (washing between with water) with

A. Methylene Blue, 0.5 Gm.

Alcohol absolute, 10 Cc.

Distilled water, 475 Cc.

Glacial acetic acid, 25 Cc.

B. Bismarck Brown,* *Syn.* Vesuvine, 1 Gm.

Distilled water, 500 Cc.

The length of time each stain is used has been much altered by various workers. Originally it was a matter of 3 seconds with A. and 10 seconds with B. The method can be used for examining direct from the swab.

The use of Eosin Solution instead of B. above gives good results, working as follows:—

1. Make film in usual manner. 2. Stain with A. three minutes, and without washing pour on Gram's iodine solution 1 minute. 3. Wash in water and counterstain with Eosin 5% aqueous solution 3 minutes, wash dry and mount. This method was claimed to be diagnostic, but other organisms, *e.g.*, *B. Xerosis*, *B. Proteus Zenkeri*, *B. Cyanogenus*, and various organisms found in water, give similar results. The granules are stained blue, the rest of the bacillus is stained by the counterstain.

Good results direct from the swab are obtained by the following:—Stain with Alkaline Methylene Blue 3 to 4 seconds, afterwards with B. above.

Pugh's (*Syn.* Ponder's) Toluidine Blue Stain.—Toluidine Blue 0.02 Gm., Glacial Acetic Acid 1.0 Cc., Absolute Alcohol 2 Cc., Water to 100 Cc. A loopful of the Stain is dabbed on the dried smear and examined as hanging drop with 1/12th inch oil immersion lens. Used for direct examination from the swab, the appearance is charactersitic. *B. Diphtheriae* appears pale blue with bright and often deeply stained red granules along its entire length, some yeasts and sarcinae also show the metachromatic markings. Hoffman's bacillus stains dark blue with a light band. Diphtheroid bacilli cannot be mistaken or confused with *B. Diphtheriae* by the method. It would be well to

*Bismarck Brown and Nigrosin are incompatible. The first is a basic dye and the other acid. Details re mahogany varnish stain.—P.J. i./26,382.

Both spirit-soluble and water-soluble Nigrosine dyes are available, the former being made by heating together Nitrobenzene, Aniline and Aniline Hydrochloride with Iron or Copper at 180—200° C. The water-soluble dye is prepared from this by sulphonating and conversion of the product into the Sodium salt. Spirit-soluble Nigrosine is a greyish-black powder used with Chrysoidine for varnishes and polishes for staining leather, whilst the water-soluble dye occurs as glistening black lumps, and is used for dyeing wool and silk grey from an acid bath.—Colour Index, 1924.

make the film, if possible, direct from the throat. A negative result is not to be considered of much value. Vincent's angina fusiform bacilli also stain dark blue. The method is claimed to be simple and rapid.—Constant Ponder, L. ii./22,23. *Stitt finds it better than Neisser's.*

Two reputed pseudo-varieties; one morphologically and in all respects similar to the specific organism, but non-virulent, the other, **Hoffmann's Bacillus**. This stains more regularly than the diphtheria bacillus and shows no polar staining. Uniform in shape, size and staining.

The general trend of opinion is that the *Hofmann Bacillus* is quite distinct, but Hewlett thinks that it really includes several species of which one may be a modified form of the diphtheria bacillus.—B.M.J. i./12,75.

It is said that 10% of people normally harbour such as against 1 to 2% with granule types.

Reports on swabs from throat and nasal passages. Presence of Hoffmann's bacillus of no clinical significance.—J. L. McCartney, L. ii./28,514,565.

Pathogenicity of true Diphtheria Bacillus compared with pseudo forms.

Five Cc. of a glucose-broth culture two days old with pseudo-diphtheria bacilli are not pathogenic to guinea-pigs, whereas $\frac{1}{2}$ Cc. of a similar culture of true diphtheria bacilli usually kills in two days.

Glucose Litmus Broth cultures of true diphtheria bacilli show marked acidity in 24 hours, while those of the pseudo forms are stated not to evince this alteration of reaction. *This method is useful for confirmation where no licence for inoculation of animals is held.*

Serum-water gives good result:—

Coagulate blood serum in an equal quantity of water, filter, add to one half 1% glucose, and to the other 1% Saccharose. Add neutral red as indicator. After 24 hours a marked acid is produced in the glucose tube by *B. diphtheria*, in both the glucose and the saccharose tubes by *B. Xerosis* (*vide infra*) and no change is produced in either tube by Hofmann's Bacillus.

B. Paralyticans longus and *B. paralyticans brevis* (**Muirhead's Diphtheroid Bacillus**).

B. Xerosis occurring in xerosis conjunctivæ, also in nose, throat and ear, differs in the fact that primary cultures from the eye on blood serum first appear in 36 hours. Sub-cultures do not show this difference. The organism is non-pathogenic to guinea-pigs.

Characters. Gram + and very similar to *B. diphtheria*: often occurs in the throat.

Koch-Weeks bacillus, a thin, non-motile organism decolourised by Gram's method, is found in a large number of cases of conjunctivitis. A diplo-bacillus has also been found which causes an extremely dangerous form of conjunctivitis, but it is amenable to treatment.

B. Morax-Axenfeld.—Angular conjunctivitis is the only form of conjunctivitis in which the clinical appearance is characteristic of the organism at work—the diplobacillus of Morax-Axenfeld (Gram-). Boric lotion and Zinc Sulphate 0.5% rapidly effects cure.

Potassium Tellurate Culture Medium has been advocated, see Edn. XVIII, Vol. II, p. 512.

Gordon and Hine's Legumin Trypagar (*q.v.*), with the addition of 0.3 Cc. of sterile 1% Telluric Acid to 10 Cc. of the Agar is a good medium for growing *B. diphtheria*. The majority of organisms other than diphtheroids reduce the Telluric Acid and produce blackish colonies. Especially is this the case with the staphylococci; the streptococci do not reduce the Telluric Acid. The diphtheroid colonies are greyish white, about 1 mm. in diam., semi-translucent, slightly convex and have a slightly darkened central spot.—D. R. Wood, B.M.J. i./21,562.

Sections of Membrane.—Stain for the diphtheria bacillus by the Eosin-Gram method:—

1. Stain 4 or 5 min. with eosin solution. 2. Wash well in water. 3. Pass through a little alcohol. 4. Stain with anilin-gentian-violet, 10 min. 5. Cover with Gram's iodine solution, 3 min. 6. Decolorise with anilin oil. 7. Clear with xylol and mount in xylol balsam.

Roux's Stain for Bacteria.—Dahlia or Gentian Violet 0.5 Gm., Methyl Green 1.5 Gm., Distilled Water 200 Gm.

Diphtheria Antitoxin, Serum Antidiphthericum.

Preparation of Diphtheria Antitoxin.

Consists of the fluid separated from coagulated blood of the horse immunised by inoculation with diphtheric toxin, produced by the filtered culture of the *Bacillus diphtheriae* in broth—a surface growth is important. Repeated injections during 4 to 6 months of increasing quantities of toxin up to as much as $\frac{1}{2}$ or 1 litre render the serum of a high antitoxic quality. When the horse's serum has acquired a sufficiently great antitoxic property, the horse is bled about 10 days after the last injection and the serum prepared for use as a remedy, and as a prophylactic.

That of P. Belg. and P. Jap. must be marked with the name of the maker, date, and rotation number, also the number of units per Cc. in the vial. Similar remarks apply in the case of the U.S. preparations. '**Concentrated Diphtheria Antitoxin**' is dealt with in Vol. I., p. 916. Keep in the dark in a cool place. P. Jap. states the serum must be sterile. This pharmacopœia has:—

(A) *Serum Antidiphthericum Liquidum*, which should possess not less than 500 units in 1 Cc. Three Classes—No. 1 contains 600 antitoxic units; No. 2, 1,000 a units; No. 3, 1,500 units. Injected subcutaneously, 0.5 Cc. should not kill a mouse of 15 Gm. weight, nor should 10 Cc. be fatal to a guinea-pig. (B) *Serum Antidiphthericum Siccum* 1 Gm. represents at least 5,000 antitoxic units.

Units of Immunity.

The Ehrlich Standard formerly laid down by France, U.S.A. and Germany at the Conference in Paris, Nov. 1922 (see Vol. I., p. 916) was recommended for adjustment and general International agreement—M.R.C. Report B.M.J. i./23,110.

The E. B. Unit refers to the toxin **neutralising power** of the serum not to the volume of the liquid. The unit of antitoxin is the amount which will neutralise 100 M.L.D. of diphtheria toxin. A standard serum is prepared for comparative purposes; 1 Cc. of this contains 1 unit of antitoxin.

The strength of sera is ascertained by physiological tests on guinea-pigs, weighing, as near as possible, 250 Gm., using mixtures of different quantities of the serum, and a lethal test dose of standardised toxin. The neutralising point is indicated by the animal's death being prevented on the fourth day.

Preservation.—There is marked loss in antitoxic value in liquid serum at room temperature,—e.g., in 2 years a loss of over 30% has been determined. Dried diphtheria antitoxin, on the other hand, kept in the dark at 5° C. retained its potency for five years.

A good **Culture medium** is bouillon with 1.5% Witte's peptone, 0.5% sodium chloride and 0.2% invert sugar. The formation of toxin is increased sixfold by the addition of 0.01 Cc. of N-manganous chloride per litre of medium, larger quantities decrease formation. The temperature limits of growth are 20° and 42°, optimum 34°; and limits of P₂ 5.2 to 8.9, optimum 7.0. The optimum P₂ for obtaining the toxin is 7.2 to 7.6 at 36°.—J.C.S.A. i./22,795,902.

No essential oil was found to be an effective germicide for the diphtheria bacillus.—P.J. ii./25,497.

References to the use of Diphtheria Antitoxin.

The earliest report of the use of the antitoxic serum (by Behring & Kossel) is found in the Deut. Med. Woch. of April 27, 1893; this is noted in B.M.J. i./93,83.

First English reported case by Eastes, 5 Cc. of Aronson's preparation in a child of 10 years, with recovery.—B.M.J. ii./94,125. Second,—p. 180.

Diphtheria of the skin—the primary seat of infection being the eyes—thence to the vulva and the lower part of the face, has been satisfactorily treated with antitoxin.

In erysipelas in some cases the injection of Diphtheria Antitoxin causes rapid fall of temperature with disappearance of skin manifestations.

Diphtheria, malignant with multiple lesions in a child six weeks old failed to respond to 12,000 units of Antitoxin.

Pigeon diphtheria has nothing to do with human diphtheria.

In diphtheritic conjunctivitis must be used early. If no response a mixed infection may be present.

1,550 cases of diphtheria—78 of which were hæmorrhagic—treated with high doses of Antitoxin. As a rule not more than 1 injection daily,—the maximum at one time rarely exceeding 24,000 units. Subcutaneously preferred.—M. P. Oct. 1909, 390.

Diphtheria Carriers are found of all ages and of either sex, the presence or absence of an obvious pathological condition is no criterion for detecting a carrier, of the length of carrier life, or of virulence. The length of carrier life seems to have no effect on virulence.—bacilli have been demonstrated to be virulent after four and eight months in the ear and nose of different individuals.

Modern methods of detection and prophylaxis, where the population concerned will allow the medical officer full scope, give practically complete control of diphtheria.—R. A. O'Brien, B.M.J. ii./28,436.

The length of carrier-life of the bacillus appears to have no effect upon its virulence since the organism has been proved to be virulent after four and eight months in the ear and nose.—L. i./12,662.

Diphtheria—review of Medical Research Council's Report, 1923.—B.M.J. i./24,439.

Schick Test in Diphtheria (introduced by Prof. B. Schick, of Vienna, in 1913).—The administration of minute doses of Diphtheria toxin. A standard diphtheria toxin is diluted at first 1:10, in 0.5% phenol; this dilution will keep in the ice box for at least two weeks. For use, further dilutions are now made in normal saline, of such strength that 0.1 Cc. contains 1/50 minimum lethal dose for the guinea pig. This amount is injected intracutaneously in the flexor surface of the arm or forearm. If antitoxin is absent or only present in small amount insufficient for protection, a circumscribed area of redness persisting 7 to 10 days is produced and on fading shows superficial scaling and persistent brownish pigmentation, the reaction showing whether the subject requires to be immunised by inoculation of a toxin-antitoxin preparation. Enables one to differentiate individuals who are susceptible from those who are not susceptible to diphtheria.

Method of conducting the test.

The standardised diluted diphtheria toxin is supplied in 1 Cc. ampoules of which 0.2 Cc. is injected intracutaneously into the left forearm. A similar amount of control, *i.e.*, toxin, *which has been heated*, is injected into the right arm. A flush, sometimes with a deeper red centre, on the site of injection into the left arm, and the absence of an identical flush on the right arm indicates a positive reaction. This develops in from 24 to 72 hours and is more easily read on or after the third day.

Immunisation. Patients who give a positive reaction, should be immunised by **Toxin - Antitoxin** or **Toxoid - Antitoxin Mixture (Diphtheria Prophylactic T.A.M.)**, of which usually 3 injections of 1 Cc. each are given at weekly intervals, though in some cases an initial dose of 0.1 Cc. is preferred.

Babies up to 6 months seem to be immune; between the ages of 6 months and 5 years the majority give a positive reaction, and the test is unnecessary—all these children may be safely injected with the toxin-antitoxin without preliminary testing. For immunisation, the toxin-antitoxin is given in 3 doses of 1 Cc. (or less) subcutaneously at intervals of 7 days. The injections are attended with some danger. Of 40 children in Vienna receiving the prophylactic injections, 6 died with symptoms of general diphtheria intoxication, and several others exhibited skin necroses. The addition of Formaldehyde (see **Ramon's Anatoxin**) renders the toxin non-toxic. It is not advisable to attempt immunisation in patients with advanced heart disease and kidney affection, or those recovering from acute infectious diseases. It is claimed that 70 to 90% of those treated are found to be immune after 8 weeks. Of 90,000 school children treated in America 14 contracted diphtheria, while in a similar number of controls 56 acquired the disease. One of the chief difficulties in the use of the test is the **pseudo reaction** due to the presence in the toxic filtrates of some substance more stable than the specific one, and which causes rise of temperature and other reactions. The toxin-antitoxin mixture should not be used after exposure to a temperature below 0° C. From 1 to 5 years is the most favourable age for diphtheria prophylaxis.—R. Munro, B.M.J. i./27,506.

Ministry of Health paper on.—B.M.J. ii./21,994. Confirmations of its utility.—Pres., Feb. '21,55.

According to a further recent M.R.C. Report, "The evidence already available leaves no doubt that the disease and its often fatal consequences may now fairly be called avoidable.—J. Graham Forbes.

Under the auspices of the Ministry of Health, the test, followed by immunisation in positive cases, has been carried out in 50,000 children in this country, and **none of these children** (except 2 or 3 especially susceptible) **has since contracted the disease**. More important to immunise children of pre-school age—the dangerous period. Recurrence of fatalities due to toxin-antitoxin mixture containing excess of toxin improbable in future owing to **substitution of toxin by the entirely non-poisonous anatoxin or toxoid**. Where possible Schick Test should be repeated three months after last immunising inoculation, as in some cases a further inoculation may be necessary. Testing and immunisation of all nurses in fever hospitals strongly advocated.—S. M. Copeman, B.M.J. i./28,833.

The test is useful in deciding whether a patient is a carrier or really suffering from diphtheria; also useful as showing to whom, among persons exposed to infection, *e.g.*, contacts, doctors and nurses, one may safely omit to give antitoxin—thus greatly minimising risk of anaphylaxis, and saving pain.—Gladys Ward, B.M.J. i./21,928.

The blood of individuals who possess a natural immunity contains, per Cc., not less than 1/30 unit of antitoxin.—B.M.J. ii./22,484.

Freezing destroys the anti-toxin in the serum and leaves only the poison to be administered. 19 students poisoned at Concord Academy, U.S.A., owing to inadvertent exposure of serum during exceptionally cold weather.—L. i./24,505.

Observations on the Test.—C. B. Ker, L. i./24,1101.

Results in Fraserburgh.—J. P. Watt, B.M.J. i./25,1035.

The Test is **of academic interest only** and should be abandoned, as it is subject to a sufficient percentage of false negative readings to result in failure of protection of children who would otherwise have been protected; also knowledge of immune status of children is not required as most of those in the age group most concerned are susceptible, while immunisation of the balance is open to no objection.—W. H. Kellogg, Am. Jl. Pub. Health, Oct., '25, per Jl. A. M. A. ii./25,1667.

Should be employed on a National scale. More economical than treatment.—E. Donaldson, B.M.J. ii./26,551.

In school practice.—W. Dunn and Co-workers, L. i./27,178.

Death of 6 children following injection of toxin-antitoxin mixture. Prof. Pirquet's advice that active immunisation be discontinued was followed by the Austrian Ministry.—L. ii./25,713,941.

The permanence of the Schick-negative state.—H. J. Parish, L. ii./28,322.

Diphtheria Toxin—Antitoxin, *Syn.* Diphtheria Prophylactic, termed 'M.M.I.'

E. von Behring at the Congress for Internal Medicine, Wiesbaden, 1913, announced that he had found a *mixture of diphtheria toxin with the antitoxins* in suitable proportions, when injected into man or animals, forms an amount of immune bodies in the blood, with the result that immunity for a considerable period is established. The reaction in man varies with age.

Anatoxin (Ramon)—As a result of investigation by J. Renault and P. Lévy, the view is confirmed that toxin and antitoxin do not form a stable compound, and that though physiologically antagonistic, each preserves its individuality in a mixture, but the antitoxin appears to deteriorate more rapidly than the toxin, so that within a few months of preparing a neutral mixture it is necessary to add antitoxin to correct deterioration. A modification of the toxin-antitoxin mixture obviates need of control, and is safe. It contains a large excess of antitoxin over toxin, the two being mixed just before inoculation, the optimum mixture for prophylaxis containing in each dose 300 units of toxin and 100 units of antitoxin (1 unit of antitoxin neutralises 100 units of toxin,—Ehrlich). Each dose consists of 1 Cc. of toxin and 0.4 to 0.33 Cc. of antitoxin. Three injections given subcutaneously at intervals of 8 days establish immunity in three to six months, which lasts for two years or longer. For therapeutic purposes, the authors employ a 2 Cc. dose of **Ramon's Anatoxin** made by incubating diphtheria toxin, to which a small proportion of Formalin has been added, for a month at 37° C.—Leader, B.M.J. ii./24,1064.

The Anatoxin is stable for long periods below 20° and resists heating for 1 hour at 65–70°. The Formaldehyde treatment has also been applied to the toxins of tetanus, botulism, gas-gangrene, toxic vegetable proteins and to cobra venom; in all cases the products ("Anatoxins") were strongly antigenic but no longer toxic.—G. Ramon, *Ann. Inst. Pasteur*, '25, 39, 1, per J.C.S., A. i./25,339. See also G. Ramon, *B.M.J.F.* i./24,44.

The intrinsic antigenic value of Anatoxin should be of at least 5 antigenic units—that prepared by the Pasteur Institute is of 8 to 10 units. Initial injection subcutaneously 0.5 Cc. After 3 weeks give a second injection of 1 Cc. and 15 days later a third injection of 1 to 1.5 Cc. (this 3rd injection is not always necessary). All children from 1 to 8 years should be vaccinated. In epidemics inject 1,000 units of antitoxin preceded by a few minutes by an injection of Anatoxin, the second and third injections of Anatoxin being given in the usual way. Nearly 300,000 persons vaccinated in France since 1926.—G. Ramon and G. I. Hclie, *Jl.A.M.A.* ii./28,1033.

Results of 1,297 inoculations with diphtheria anatoxin.—*Jl.A.M.A.* ii./25,472.

Injection of 2 to 3 Cc. of antitoxin mixed with anatoxin 2:1 conferred an active immunity on rabbits and guinea-pigs, while no immunity could be obtained from anatoxin alone, nor from mixture with normal serum free from antitoxin.—*Comptes Rend.*, per *Jl.A.M.A.* ii./25,1009.

Ramon's anatoxin as prophylactic among school-children. Those showing strong positive reaction received 0.5 Cc. subcutaneously and 3 weeks later 1 Cc. Schick Test after 3 weeks showed 95% immunity. *Paris Med.*, May, '26,456, per *Pres.*, Jan., '27,14.

Purified Diphtheria Toxoid.—Culture filtrates containing Toxins treated with Formalin are partially or completely converted into Toxoids. The *Ramon Flocculation Test* being used for assaying strength of the fractions, the 'Langstaff dose' being the amount of toxin equivalent to one unit of Antitoxin by this test.—A. F. Watson and E. Langstaff, *Wellcome Physiological Research Laboratories Report*, 'Biochemical Journal' (Vol. XX., No. 24, p. 763.)

Diphtheria Endotoxin.—*Dose.*—0.5, 1 Cc. and if required 1.5 Cc. at intervals of about 7 days in the muscle of the upper arm or back.—R. T. Hewlett, *L. i.*/15,275.

Made by Macfayden's washing, centrifugalising and grinding method. The treatment, given while the membrane was still present on the tonsils, resulted in freedom from diphtheria bacilli on the fauces in several cases in ten days to a fortnight from date of injection, whilst ordinary cases of faucial diphtherias are not as a rule free from infection for a month or five weeks after the onset of the attack. In other cases there was a distinct diminution in the number of bacilli present. The Endotoxin is not intended as a substitute for Diphtheria Antitoxin,—the latter is to be used in the treatment of the case in the ordinary way. Animal experiments show that the Solution in above strength possesses considerable protective power against injections of living *B. Diphthericæ*. It was found that even after keeping 2½ years the Endotoxin was active.—R. T. Hewlett and A. T. Nankivell, *L. ii.*/12,143; *L. i.*/13,1802.

"Positive Throat" in diphtheria convalescents treated by stock Vaccine. *Dose* 10 to 200 million. Well defined degeneracy in morphological appearance of the cultured organism followed by complete dispersal from the locality invaded.—J. L. Brownlie, *L. i.*/20,706.

UNTOWARD RESULTS, SERUM RASHES, ETC., WITH DIPHTHERIA ANTITOXIN.

The symptoms of Diphtheria Serum Sickness are fever, rash, usually urticaria or a variety of erythema multiforme. Sometimes more unpleasant effects, namely, pains in joints, tendons and fasciæ with fever occur.

A case in which 3,000 units produced œdema and an urticarial eruption. 20 grain doses of Calcium Chloride every 2 hours—swelling disappeared in 14 days.—*B.M.J.* ii./09,95.

Asthmatic patients should receive injections with caution, even as prophylactic.

Intense itching, subsequently vomiting, has been cured by 1/6 grain Morphine.

Death following diphtheria antitoxin intravenously—due to status lymphaticus, not anaphylaxis.—D. MacIntyre and D. W. McKay,—*L. ii.*/23,1133.

Profuse hæmorrhage in diphtheria.—A boy aged five treated by several

4,000 units of Antitoxin by the mouth, in addition injections of 2,000 and 4,000 units. About $1\frac{1}{2}$ pints of blood were passed with membranous casts. One piece more than 2 ft. long. The *prima via* was clearly implicated and the topical use of the Antitoxins was successful.—W. F. Clark, B.M.J. ii./13,1484

Dysentery.—There are two main types of dysentery—Amœbic and Bacillary (cf. *Vol. I.*, pp. 526, 917, 918).

To search Stools and Mucus for *Entamoeba Histolytica*.—

In *searching mucus* for *amœbæ* stain with a little Methylene Blue and examine with low power, e.g., $\frac{1}{2}$ inch—turn on the $\frac{1}{8}$ inch to verify. *Amœba Coli* occurs very seldom.

Alternatively,—place a small piece of freshly passed stool on a slide, adding one or two drops of 1 in 10,000 Neutral Red in Normal Saline. Examine with $1/6$ th inch objective. The Amœbæ take up the Neutral Red,—all other constituents of the fæces,—even the leucocytes—remaining uncoloured.

Differential Diagnosis.—Characteristic cellular exudate in the stools of amœbic and in bacillary dysentery. The finding of *E. histolytica* in the midst of a “bacillary” exudate of this kind indicates that a double infection is present, although attempts to isolate dysentery *bacilli* may fail.—J. G. Willmore and C. H. Shearman, L. ii./18,200. See also G. M. Findlay, L. i./19,135.

Notes on etiology of dysentery. *E. histolytica* in 63 cases out of 217 and *B. Dysenteriae* (Shiga) in 47.—C. J. Martin, B.M.J. i./17,479.

Amœbic dysentery practically disappeared from the Panama Canal Zone following the installation of a pure supply of water.—U.F.C., '25,115.

There are said to be nearly 2 million *E. histolytica* cyst passers in England.—L. ii./26,762.

J. W. Cropper and R. W. H. Row describe methods of concentration of cysts from stools:—

(1) **For Diagnosis.** Shake a lump of fæces (at least 1 Gm.) in about 30 Cc. of normal saline preferably with a mechanical shaker in a large flask or bottle for $\frac{1}{2}$ hour. Then transfer to a separating funnel and shake by hand for $\frac{1}{2}$ minute with 10 or 20% of its volume of ether. Allow to stand for a minute or two. The cysts remain in the saline, fæcal debris rising in a mass at the top of the saline, immediately below the excess of ether. The saline is removed and centrifugalised. The sediment in the centrifuge tubes would be some 15 times as rich in cysts as the original matter. If desired this can be again shaken up and centrifugalised afresh.

(2) **For Cultivation.** A modification of Penfold, Woodcock & Drew's process (B.M.J., May 20, '16) does not employ ether and is therefore more suited for cultivation purposes.

10 Gm. of specimen are shaken with 100 Cc. of saline in a mechanical shaker 5 minutes and poured on a fine silk of mesh $40\ \mu$ stretched on a tambour. It is gently stirred with a rod and the filtrate or a portion of it is centrifugalised one minute at 1200 revolutions per minute, the supernatant liquor poured off and the volume made up again with normal saline. Shake and again centrifugalise. Repeat until the supernatant liquor is almost clear. Finally shake the deposit with 10 Cc. normal saline and allow to stand for 10 minutes. The upper portion is then poured off and thoroughly centrifugalised and loopfuls used for making hanging-drop preparations for cultivation. For counting Botcher's slides are used.—L. i./17,179.

No purgative should have been given for some days otherwise the precystic forms, difficult to identify, will be present. Examination during Emetine administration is useless.

For *amœbæ* mix a small piece of mucus with normal saline and examine unstained under $1/6$ " objective.

For cysts and precystic forms emulsify a little of the stool (1) with saline and (2) with 1% aqueous solution of Iodine in Potassium Iodide.

Characteristics of *E. histolytica*.

The entamoeba varies in size from 6 to 35 μ . though usually being 2 to 3 times the diameter of a leucocyte, i.e. about 12 to 24 μ . Red blood corpuscles, bacteria, cells, etc., may often be seen in the interior though the ingestion of red corpuscles is by no means a constant factor. The organism can, according to Rogers, only rarely be found in pus, but is always present in scrapings from the wall of the abscess. The amoeba passes through the intestinal wall and on reaching the submucous layer forms an abscess. Hewlett says the organism may be cultivated on ordinary agar if an organism, e.g. *B. Coli*, be present. For a description of this and other amoebæ see Medical Research Com., B.M.J. i./17, 669; also H. A. Haig, L. ii./19,823; and J. S. White, P.J. i./15,797.

Comparison with *E. Coli*.—The following table shows differences from *E. coli*, which is so commonly found in fæces. Actual measurement of size is a great help. Amoebic diarrhoea should never be diagnosed on precystic forms alone.

	<i>E. histolytica</i> .	<i>E. coli</i> .
Active forms	Size 20 μ to 30 μ . Clear ectoplasm, granular endoplasm Red blood cells included Sudden explosive movements Eccentric inconspicuous spherical nucleus with small central dot.	Size 20 μ to 30 μ . Ectoplasm and endoplasm both granular. Bacteria, yeasts, vegetable cells included Movements very slow and no locomotion Central conspicuous nucleus with an eccentric dot.
Pre-cystic forms	Size 7 μ to 14 μ Round Ectoplasm and endoplasm not differentiated No inclusions No movements Nucleus a beaded ring. May be elongated and undergoing division.	Almost impossible to distinguish from <i>E. histolytica</i> .
Cysts	Size 7 μ to 9 μ , or 11 μ to 14 μ 1, 2 or 4 nuclei Mature cyst has 4 nuclei Mature cyst contains glycogen.	Size 15 μ to 20 μ 1 to 8 nuclei Mature cyst has 8 nuclei Mature cyst contains no glycogen.

Many cases of diarrhoea or colitis might be found to be amoebic in origin if the stools were systematically examined.—L. E. H. Whitby, Midx. Hosp. Jl., Mar., '25.

E. histolytica **cultivated** by Böck and Drbohlav. In culture *E. histolytica* feeds on bacteria and red blood cells whenever the latter are present in the medium.—Proc. Nat. Acad. Sc., May 15, '25, 239, per Jl.A.M.A., July 18, 25, 196. See also Am. Jl. Hygiene, 1925, CCCLXXI., L. ii./26,762, and Y.B.P., '27,79; and detection in fæces, *ibid.* 80.

***E. Coli*.** *Syn.* Amoeba Coli of Losch. Occurs in the upper part of the large intestine. It appears to be harmless. According to Schaudin it differs from *E. Histolytica* in that the ectoplasm is not distinctly seen except during the formation of a pseudopodium and the nucleus stains deeply. It never takes up red cells. *E. Coli* multiplies by binary fission and also by multiple fission into 8 small amoebæ. *E. Histolytica* produces an indefinite number of small amoebæ.—J. S. White, P.J. i./15,797. For further differences see *E. Histolytica*.

Entamoeba Nana (Wenyon & O'Connor) inhabits the human intestines in addition to *E. Coli* and *E. Histolytica*. *E. Nana* is a small amoeba measuring when rounded 6 to 12 μ . The cysts are very resistant. No evidence that it is pathogenic.—C. Dobell & Margaret W. Jepps, B.M.J. i./17,607.

***Lambli*a infections.** Three cases in men who had never been out of England. Circumstances of infection not known.—A. Malins Smith & J. R. Matthews, B.M.J. ii./16,389.

These parasites are very troublesome to remove. The best results were obtained with Beta-Naphthol 15 grains and Bismuth Salicylate 20 grains thrice daily. Turpentine in 10 minim doses tried but not so useful.—B.M.J. ii./16,407.

Transmission of Intestinal Protozoa experiments. Amœbic Dysentery is possibly dust-borne. Stephens' Scarlet Ink used for staining purposes.—J. C. Watt, L. i./20,543.

In diagnosis of chronic dysentery by means of the sigmoidoscope the large bowel is emptied by means of $\frac{1}{2}$ ounce of Castor Oil in the evening, followed next morning by a soap and water enema, immediately after which 15 minims of Tincture of Opium is given. The distance the instrument can travel varies—up to 12 ins. has been passed.—P. Manson-Bahr and A. L. Gregg, per T.D.B. 18/21,35.

The diagnosis of intestinal amœbiasis assisted by provoking an artificial relapse with Keratin coated capsules of Bile Extract, 0.2 Gm., 3 after each meal. The stools become fluid and organisms and cysts observed in large numbers.—Le Noir and de Fossey, per T.D.B. 19/22,688.

Flagellate dysentery.—A survey of the literature of flagellate dysenteries, it is stated, leaves the mind of the reader in a turmoil as to their pathogenicity or otherwise. Few admit the presence of flagellates in the bowel as anything more than a coincidence, when found along with dysenteric symptoms. Others credit *Lambli*a *intestinalis* with pathogenic effects and still leave *Trichomonas intestinalis* and *chilomastix mesnili* in the coincidence group. An analysis of 716 cases showing these and other infections. Purgation, Thymol, Emetine, Bismuth Iodide and colon lavage valuable. Flagellate dysentery can be cured in at least 50% of cases.—H. G. Whittingham, B.M.J. i./23,799.

Giardia lamblia, *Trichomonas hominis* and *Chilomastix mesnili* are probably the real etiological factors of "flagellate diarrhœa." Carnivorous animals are rarely infected with intestinal protozoa; a carnivorous diet is unfavourable to giardias and trichomonads of rats, and such a diet may also be unfavourable to these flagellates in man. Diarrhœic patients so treated have shown either an extremely marked diminution in the number of flagellates or a total riddance of them.—R. W. Hegner, Int. Conf. Trop. Am., '24,404.

The spread and incidence of protozoal infections in the population of this country. As the result of examination of nearly 3,000 people, including army recruits, adult civilians, children under 12, and asylum patients (none of whom had been out of England, with the exception of a very small percentage in the last group), *E. histolytica* was found in every section of the population, establishing the wide occurrence of the infection in this country, and showing that it is no longer necessary to presume foreign origin for any home case of amœbic dysentery or for any infection with *E. histolytica*. Indigenous cases of acute amœbic dysentery do occur in England and may be more common than has been supposed—possibly concealed under such names as "hepatitis" or "ulcerative colitis."—A. Malins Smith, B.M.J. ii/24,897.

Systemic infections by *E. dysenterice*. From its portal of entry through the epithelium of the colon into the submucosa, *E. dysenterice* tends to spread in the margins of ulcers of the colon into capillaries and smaller veins and thence may make its way into the capillary net of the liver, through the heart to the capillary net of the lung, and thence to the systemic circulation. Liver, lung and brain abscesses are thus interpreted as hæmatogenous invasions by way of the blood stream—as is also infection of bone-marrow. Following the finding of *E. dysenterice* in the stools of 18 out of 20 cases of Hodgkin's disease, the authors infer that this disease is amœbiasis of the lymphatic system, the amœbæ arriving at these locations by the systemic circulation, or possibly the lymphatic system. Resistent cysts discharged in the fæces the sole mode of infection, the agencies causing contamination being the soiled hands of food-handlers and flies.—C. A. Kofoed and Co-workers, Int. Conf. Trop. Am., '24, 381-397.

Councilmania lafleuri, an amœba of man, has clear pseudopodia, eats red blood corpuscles and has a very marked resemblance to the motile forms of the amœbæ of dysentery. Its cysts have 8 nuclei

resembling those of *E. coli*, but differ from them in the larger subdivided central karyosome of the nucleus. It is wholly resistant to all forms of Emetine treatment and as it often occurs coincidentally with the amœbæ of dysentery and persists after the extermination of the dysenteric infection it might give a misleading picture of the failure to cure by the Emetine treatment. Presence invariably revealed by its characteristic cysts but motile stage separated with difficulty from that of *E. dysenteriae*.—C. A. Kofoid, Int. Conf. Trop. Am., '24, 327.

According to the Annual Report on the Health of the Army for 1925 nearly all the cases of dysentery in Iraq were amœbic, whereas only one of the cases in Turkey was of that type, and in Egypt 35 out of 64 cases were amœbic.—B.M.J.i./26,202; K. Boney queries these figures.—*ibid.* 303.

Bacillus Dysenteriae.—The dysentery organisms are divisible into two main groups. According to a Medical Research Committee Report, *B. dysenteriae* (Shiga) and *B. dysenteriae* (Flexner), it is universally agreed cause bacillary dysentery—short rods, destitute of flagella, and non-motile, Gram negative, fermenting Glucose without gas formation and producing alkali in milk.

Shiga's organism is relatively well defined. It does not ferment Mannite, does not produce Indol in Peptone Water. It is highly toxic to man and animals. It is a distinct and separate species. The Flexner group produces acid in mannite and + or —Indol in peptone water.

Flexner's, however, is separable into several distinct strains. Details.—F. W. Andrewes, F.R.S., and A. C. Inman, Serological Races of the Flexner Group, Med. Res. Com. Rep., Series No. 42. L.i./18,560; i./20,162.

The bacilli of Shiga and Flexner are non-motile, non-sporing, and do not stain by Gram's method and grow on all ordinary media. In cultural characters they resemble *B. coli communis*.

The close relation of the prevalence of infantile diarrhœa mortality and the prevalence of flies is shown in a number of diagrams of plotted curves which are wonderfully coincident. Insect porters of bacterial infection.—C. J. Martin, L. i./13,181.

DYSENTERY CARRIERS (See also Vol. I., pp. 528, 532, 1055).—Healthy carriers are very rare and of no importance. Actual carriers are to be found among the incomplete convalescents which form a high percentage of the cases. In combating an epidemic it is necessary to reduce as far as possible the number of such cases and to isolate very strictly those that are already of this type.

The dysentery bacilli have an exotoxin and endotoxin. The former is a neurotoxin; the latter acts as a poison on the intestine. By the suppression through anaerobiosis of the exotoxin-producing activity of *Bacillus dysenteriae* Shiga, a pure endotoxin is produced directly from the culture.—J. E. McCartnet and P. K. Olitsky, per J1. Trop. Med., Aug. 1/23, 259.

In colitis a new bacillus found constituting a third group of dysentery bacilli. Pathogenic for man and animals. Easily confused bacteriologically with Flexner-Y type, but slow fermenter of lactose.—S. W. Patterson, per J1. Trop. Med., Feb. 15/23, 64.

Bacillus meta-dysentericus (Castellani)—virulence of. Results of experiments on rabbits. Its virulence less marked than that of *B. Shiga-Krusel* while having an apparently similar toxin. Resistant to direct sunlight for 1½ to 2 hours, and still alive after 6 hours exposure to diffused light.—G. Olivi, J1. Trop. Med., April 16/23, 123.

Dientamoeba Fragilis (Jepp & Dobell). A case of human infection in England.—J. G. Thomson and A. Robertson, J1. Trop. Med., May 1/23, 135.

Dysenteries of India.—H. W. Acton and R. Knowles, I.M.G., July, 24/325.

Serum Diagnosis of chronic bacillary dysentery. Standard agglutination tests with Shiga-Flexner groups of dysentery cultures may have large field of usefulness in helping to determine prevailing type of infection, allowing of treatment by dysenteric vaccines, made up of organisms corresponding to prevailing types (Thomson's Detoxicated Vaccines). Standard agglutination tests may possibly be of value even in diagnosis of chronic dysentery.—E. H. R. Altounyan, L. i./24, 75.

Dysentery Anatoxin. The preparation and use of.—Ann. Inst. Pasteur., Feb., '26, 134, per Pres., Jan., '27, 16.

Anti-dysentery Bacteriophage. Encouraging results with, in bacillary dysentery—70% of cases gave rapid improvement.—A. Compton, L. ii/29, 275.

Encephalitis—Inflammation of the brain.

'Post-Vaccinal Encephalitis.' A fatal case, after primary vaccination of a boy *aet.* 14, with Government lymph, 4 insertions, 3 of which 'took well.' Patient died 16 days after vaccination, duration of illness being 6 days.—G. N. Grose, L. ii./29,381: *cf. ibid.* i./29,221, and B.M.J. ii./29,324.

Epidemic encephalitis (previously called **Encephalitis lethargica**). Of this disease 5,000 cases were reported in England and Wales in 1924 and 1,025 in 1923. A large number of mild cases pass unrecognised—a truer estimate for 1924 would probably be about 50,000. **Parkinsonism**, a form of paralysis agitans, is a common sequel even in young children—characterised by rigidity of musculature of body, face becomes devoid of expression, speech affected; as stiffness increases patient unable to feed or dress himself and finally may become bedridden. Further sequelæ are neurasthenia, intractable insomnia and disturbances in respiratory mechanism. Moral degeneration often follows the disease. The causal organism is a filter-passing virus. Symptoms sometimes like influenza for which it is often diagnosed. Sleeplessness, restlessness, derangement of vision, severe pains, incessant hiccup or tendency to sleepiness may be symptoms of acute attack.

See also Lecture on "Parkinsonism," by D. McAlpine, to Inter-State Post-Graduate Assembly of America, London, June 3, 1925.

Up to October, 25th, 4,605 cases of encephalitis lethargica were notified for the year 1924, the urban districts showing greatest incidence, and the first three months of the year are recognised as the epidemic ones. The disease shows marked resemblance to acute poliomyelitis in methods of infection and general behaviour. *Whilst the view is held that acute poliomyelitis, cerebro-spinal fever, and encephalitis lethargica are independent entities, the resemblances indicate that they belong to the same epidemiological family tree and the study of one may clear up the nature of the other.*—A. S. MacNalty, L. i./25,594.

Infection may be due to the damaging of the nasal mucous membrane by a catarrhal organism, so that when inhaled the virus of encephalitis passes through and is absorbed into the brain via the perineural lymphatics.—A. L. Yates and S. Barnes, L. ii./25,130.

Intraspinal injections of autoserum gave good results in epidemic encephalitis.—per Jl. A.M.A. ii./25,1095.

Patients may recover from the severe acute attacks, from the respiratory symptoms and from behaviour and other residual sequelæ, but rarely, if ever, from the Parkinsonian syndrome.—L. H. Ziegler, Jl. A.M.A. ii./28,141.

See also our Vol. 1, p. 1057 and **Poliomyelitis** this Vol. p. 567.

Filariasis.—In *Filaria sanguinis hominis* infection or elephantiasis. Larvæ only of *Filaria* occur in the blood. The worm itself is subcutaneous. Elephantiasis in all its phases is very marked in some localities. *C. quinquejasciatus*, *Aedes variegatus* and *A. albopictus*, *Anopheles rossi*, *Anoph. ludlowi* and *Anoph. costalis* are proven vectors. Sheathed embryos of the filaria are taken up by *Culex* and the larvæ in due course reach the definitive host (man) through the intact pores of the skin (Bahr).

The female adult worm was discovered by Bancroft, the male by Aranjol and the embryo by Demarquay and Lewis. The adult worms inhabit the lymph channels of the lower extremities and the scrotum. They lead to dilatation of the lymphatics, to hyperplasia of the tissues, chyluria, hæmaturia, abscesses, and occur in the circulation at night.

Filariasis (*F. bancrofti* infection) with plenty of embryos present in the right blood treated with Antimony Tartrate intravenously—no effect (contrary to Rogers).—G. C. Low and A. L. Gregg, L. ii./20,551.

Sir P. Manson has a thorough Chapter on Filariasis in his "Tropical Medicine." The nomenclature of the parasites has undergone revision. The filarial periodicity and the anomalous non-periodic types are dealt with.

Carbon Tetrachloride intravenously and intramuscularly has been tried in animals and suggested in Loa-loa.—S. Adler, Ann. Trop. Med., Oct. 13, 1923.

The "Blinding Filaria" of Guatemala (*Onchocerca caecutiens*, Brumpt, 1919).—F. Fülleborn, Int. Conf. Trop. Am., '24, 241-255.

Gas Gangrene.

Gas Gangrene is caused by *B. Aerogenes Capsulatus*—the Bacillus of Welch—often in association with other organisms.

Bacteriology.—Sir A. E. Wright and his co-workers concluded that the growth of the bacillus does not necessarily turn on the presence or absence of oxygen, but rather on a mechanical factor which appears to be the presence of some hole to serve as a nidus in which the microbe can concentrate its chemical effort at first upon a fractional portion of the culture medium. Clinically the supervention of gangrene is very frequently correlated with leaving infected pieces of clothing in wounds.

The toxæmia of gas gangrene is an acidæmia but the organisms also secrete specific toxins. The production of acid probably proceeds not only in the infected parts but also in the liver and other internal organs. Sodium Lactate 20 Gm. injected effected rapid cure and 10 Gm. of Sodium Bicarbonate intravenously improved, with ultimate recovery.—L. i./17,1, and B.M.J. i./17,53.

Temporary increase in immunity might be effected by a vaccine of the organism and the streptococcus, sufficient to prevent spread of infection into the tissues. Large doses of *B. Aerogenes Capsulatus* (up to 1,000,000,000) can be injected without reaction.—A. Fleming, L. ii./15,376,640.

Hydrogen Peroxide B.P. strength made neutral or slightly alkaline with Sodium Bicarbonate injected into infected wounds around the infected area saved limb.—A. A. Martin, B.M.J. i./15,145, but the procedure has been followed by death from gas embolism. Local use of Hydrogen Peroxide and Iodine Tincture recommended.—B.M.J. i./17,465.

The anaerobic organism causes an inflammation characterised by great swelling and copious sanious discharge full of bubbles or gas, is greatly assisted by the presence of staphylococci or other bacteria, and its activity is enormous. Effect produced within 5 hours of a wound. Effects of Dakin's and Lorraine Smith's Hypochlorous solutions respectively equally good.—B.M.J. ii./15,913.

Self-inoculated *B. Aerogenes Capsulatus* treated with 25 Cc. of 1½% **Quinine Hydrochloride Solution** injected intramuscularly; 10 hours afterwards 30 Cc. Within 24 hours marked local effects were produced. At the end of 48 hours patient recovered and temperature reached normal.—K. Taylor, L. ii./15,977; i./17,294,306.

B. aerogenes capsulatus, *B. œdematis maligni* and *B. tetani* isolated from gangrenous wounds. Morphology. Staining reactions.—H. R. Dean and T. B. Monat, B.M.J. i./16,77.

The *B. Welchii* is a normal inhabitant of the intestines of adults and sometimes in small numbers in the stools of infants. If in excessive numbers and if the diet contains an undue amount of fermentable carbohydrate diarrhoea is likely to result. Give a diet rich in protein instead of one rich in carbohydrate.—J. P. Symonds, Rockefeller Inst. Monograph, Sept. 27, '15 B.M.J. i./16,102.

Infection of wounds by gas producing organisms—either that of malignant œdema or by *B. aerogenes*.—A. Mackenzie Forbes, B.M.J. i./16,369.

Natural history of septic wounds—an exhaustive paper. Preponderance of anaerobic organisms: *B. œdem. malign.*, *B. perfringens* and *B. Hibler*. Small incidence of *B. tetani*. The wounded tissues contain anaerobes months after the original injury. The activity of the anaerobes depends to a great extent on their symbiosis with aerobes. Vaccine therapy important and urgent in prevention of "flares" after operation and in prevention of sinus formation and secondary hæmorrhage.—Sir K. Goadby, L. ii./16,89. A mild vaccine of sensitized polyvalent *Streptococcus* 5, with *B. proteus* 10 million, to be given pending bacteriological report. In case of gas gangrene *Strepto.* vaccine combined with *B. proteus* and *B. lactis aerogenes* to be given—10 million each, repeated on the third day.—Special Section, Vaccine Therapy, Sir K. Goadby, *ibid.* 585.

A polymicrobial invasion of aerobes and anaerobes. At one time it may be *P. perfringens* or at another the *Vibrio Septique*, Vincent's organism (causes hospital gangrene), *B. Coli* and others. Some cases show gangrene without gas formation and give gas without gangrene. As to the incubation grave forms start 24 to 48 hours after the wound, while slow forms begin on the fourth day. Alum compresses, also saturated ether solutions of camphor

advocated—Ferric Chloride, Quinine Hydrochloride, Ether, Camphor and other substances also gave good results.—Fr. Guérmonprez, B.M.J. ii./16,663.

B. Perfringens (a name used by the French) practically always present in discharges and tissues of all wounds in the war. In 2 to 5 days slight swelling develops and presence of gas in the tissues can be detected. Copper coloured mottling of the skin occurs adjacent to the wound with foetid odour. Hypochlorite washing with aid of fenestrated tube described and advised. Wright's Saline successful in selected cases, but the majority of progressive cases require surgical treatment.—Fauntleroy, B.M.J.E. i./16,24.

B. Welchii, though usually considered an anaerobe, will grow freely in open narrow tubes. It grows vigorously in liquid medium when Nitrogen containing 1% Oxygen is bubbled continuously through the tubes, but it is inhibited by higher proportions of oxygen.—C. G. L. Wolf, C. M. McGill and J. E. G. Harris, I. ii./17,787.

B. Multifementans tenalbus isolated from a case.—J. L. Stoddard, L. i./19,12.

B. tumefaciens, a new pathogenic anaerobe from.—W. J. Wilson, L. i./19, 657.

Eusol has been employed (Vol. I., p. 46); see also Quinine Hydrochloride, Vol. I., p. 728; and Specificity in Antiseptics, this Vol.

B. sporogenes—This organism differs from the gas bacillus (*B. Welchii*) and the *Vibrio septique* in being actively proteolytic whereas they act on carbohydrates rather than on proteins. Next to the gas bacillus it was the organism most frequently encountered in war wounds and was regarded as the main cause of their foul odour. Like the gas bacillus, it is often found in human or animal faeces and in fertilised soils.

It is a bacillus with rounded ends ($5 \times 0.8 \mu$), actively motile, and Gram-positive; it liquefies gelatin and digests blood serum. It does not seem to be pathogenic but appears to exalt the virulence of the gas bacillus.

It is a common contaminant of other anaerobic cultures and since its spores are highly resistant it is difficult to separate it from others. Metchnikoff's organism, the Reading bacillus, *Bacillus XI.*, and—by some—Koch's organism of malignant oedema are regarded as identical with *B. sporogenes*.—Stitt.

Braxy. This disease in sheep is an example of a pure infection with an anaerobe—a stomach infection. An injury from the lowering of the tissue defences from chills, frosted food, etc. The anaerobe invades the system in pure culture. In braxy, had it been known during the war, is to be found one of the most important of the gas gangrene organisms; other anaerobes and aerobes are left behind in the invasion—a natural purification of the bacillus by animal passage. Anaerobic infections, from the war standpoint, are of extreme importance.—Professor S. H. Gaiger, B.M.J. ii./22,962.

Glanders.

Mallein—A growth of the glanders bacillus in glycerinated broth, corresponding exactly in mode of preparation to Koch's original tuberculin. This vaccine is used as a test for the presence of glanders in sick horses, and has been injected for the cure of chronic glanders in man. The Mallein of the Lister Inst. for animals is injected in dose of 1 Cc. for diagnostic use subcutaneously in the neck over vertebræ about midway between jaw and shoulder, complete reaction is a rise in temperature of 2.7° F. after 12 to 20 hours and an extensive hot and painful local swelling.

Should the rise in temperature not exceed 1.0° C. or 1.8° F. or the size of the swelling not exceed 3 inches in diameter in 24 hours, the freedom of the animal from glanders is highly probable.

The temperature reaction is unreliable in all cases in which the temperature at time of inoculation is 2.5° F. above normal. In such cases, if there are any suspicious clinical signs to assist, reliance may be placed on the occurrence of the local swelling.

Human Glanders. Mallein satisfactorily employed in dose of 10 to 15 minims,—difficulty of diagnosis owing to close resemblance between the ulceration and the tertiary syphilitic ulceration of the buccal and pharyngeal cavities.—B.M.J. i./09,319.

A case with death.—L. ii./20,941.

The old name for glanders, malleus, is to be traced to Aristotle, being derived from *μῆλός* = bad disease or epidemic. Intradermo-palpebral test is the most popular. Watson and Heath (America) have shown that the horse can be

hyper-immunised by repeated inoculations of Mallein, and several very serious human cases have been treated with the serum in Canada with dramatic results.—B.M.J. ii./24,530.

Melioidosis in Malay. A disease of rodents communicable to man. Resembles glanders and is usually fatal. *B. Whitmorei* the causative organism.—A. T. Stanton and W. Fletcher, L. i./25,10.

Gonorrhœa.

RECOGNITION :

The *Micrococcus Gonorrhœæ* is a medium sized diplococcus; reniform in shape, in groups, intracellular character. This point is thought to be of no value in differential diagnosis, though previously stated to be so (*vide later*). The organism is Gram negative.

The following is suggested to prevent error in Gram's method :

Take a small amount of debris from the gum tooth margin with a toothpick and spread near the right upper corner of the slide to cover a circular area of 0.5 cm. in diameter. Spread the material to be examined in the centre of the slide and treat the entire slide as if it contained one specimen. Place a drop of immersion oil over both smears and examine test specimen in corner first; as this will always contain both gram-positive and gram-negative organisms there should be a sharp contrast between the blue-black of the former and the pinkish-red of the latter if the staining is satisfactory. One can thus state with assurance whether the organisms in the main specimen are gram-positive or gram-negative.—E. W. Hirsch, JI.A.M.A. ii./28,246.

See also M.R.C. Directions *postea*.

Cultivation.

Comparative Tests (under the Medical Research Committee) showed that (1) Thomson's Human Plasma-Glucose Agar (2) Coles' Tryptic Blood Agar, (3) Gordon & Hine's Trypsinised Pea Extract Agar were satisfactory for cultivation. The last is for the meningococcus (*q.v.*) and if made of reaction +6 (Eyre's Scale) instead of +1 it would be improved for the gonococcus.

Human Plasma-Glucose Agar.

To nutrient agar (2.5%) rendered +6 acid add Sodium chloride 9 Gm., calcium chloride 0.25 Gm., potassium chloride 0.42 Gm. per litre and glucose 2.5%. The sterile tubed agar is melted in boiling water, and after cooling to about 50° C. add 1 Cc. of human plasma to each tube and mix thoroughly by rolling the tube between the palms. For plating, the contents of three tubes may be added to a Petri dish.

To obtain Human Plasma.—Draw off three-quarters of a test-tube-full of blood with sterile precautions. Fill a sterile centrifugal tube, containing 2 Cc. of 2% sodium citrate solution, with the freshly drawn blood. Plug with a sterile cork (keep the corks in alcohol and burn off the alcohol before plugging) and centrifugalise. Pipette off the serum with a sterile 10 Cc. pipette and add 1 Cc. to each tube of agar as stated. (If the test-tube of blood is three-quarters full there is sufficient left for the Wassermann test.)

Using this medium the growth is profuse even in 18 hours.—D. Thomson, B.M.J. i./17,869.

Isolation of gonococci may be effected from the fluid of gonococcal arthritic joints. It is not easy to obtain the gonococcus from the blood, although cultures are often obtained therefrom; when urethritis has ceased and fluids have disappeared from the joints, one proceeds by drawing 2 Cc. of the blood, with aseptic precaution, from the median basilic vein, mixing with double the quantity of Agar Agar and plating immediately.

Milk Broth or Milk Agar.

Fresh milk 1,000 Cc. is mixed with 5 Cc. of 1 in 4 Hydrochloric Acid and kept at 37° C. for 16 to 20 hours to precipitate Casein, or the milk can be boiled, filtered and the filtrate neutralised with 10% Sodium Hydrate—then place in autoclave 2 hours, boil, neutralise again and filter. The filtrate is mixed with equal parts of broth, or one or two parts of 'Agar.' Put into test tubes and sterilise.—J. E. R. McDonagh.

For Cole & Onslow's Tryptic Broth (& Agar), see *B. Typhosus*.

For Milk Serum (Sabouraud & Noire).—See Edn. XVIII., p. 522.

Swartz's Medium made of veal and operating by cultivating in reduced oxygen tension and **Hall's Testicular Infusion Agar** are described by Stitt.

Diagnosis of Gonococcal Infections (from Med. Res. Com. Rep. No. 19, 1918; see also B.M.J. ii./18,317).

Films made from discharge in a frank case of acute gonorrhoea are characteristic as regards the intracellular position of the gonococci but diagnosis can *not* be based on presence or absence of intracellular diplococci. For official purposes **Gram's method** of staining must be used.

In decolorising, *Absolute Alcohol* must be used, i.e. 98% or over. *Weak Alcohol* decolorises Gram positive organisms. It should not be used for more than 2 minutes.

W. Jensen of Copenhagen discards the use of Aniline Water, (2) increases the strength of the Iodine solution, and (3) counter-stains with Neutral Red.

After making the film in the ordinary way, fixing and cooling—

Stain with 0.5% Aqueous Methyl Violet (6B) $\frac{1}{2}$ to $\frac{1}{4}$ minute. Pour off the bulk of the stain and wash away the remainder with a drop or two of *strong* Lugol's Solution (Iodine 1, Potassium Iodide 2, Water 100). Do not wash off with water. Pour on a fresh quantity of the Lugol and leave $\frac{1}{2}$ to 1 minute. Wash with *Absolute Alcohol* and pour on a fresh quantity of it moving the slide from side to side as in developing a photo plate. (A third washing may be necessary to complete decolorisation.) Finally rinse with a few drops of Alcohol and without washing in water stain with

Neutral Red Solution. Neutral Red 1 Gm., 1% Acetic Acid 2 Cc., Distilled Water 1000 Cc. (made stronger if necessary), for 15 seconds to 1 minute.

Wash in water, dry and mount. The gonococci take up the red dye.

Examination of Urine for Gonococci, see page 390.

Pyronin Stain, Syn. Pappenheim's or Unna's Stain.—Concentrated Aqueous Pyronin Solution 1, Concentrated Methyl Green Solution 3, is useful. Stain 5 minutes, wash and dry. Gonococci stain red, cells, etc., blue.

Wyatt Wingrave's Modification = Pyronin (water soluble) 2, Methyl Green 3, Distilled Water 100. Dissolve separately, mix and filter. After staining, wash with water and differentiate with 5% Resorcin in Alcohol.

All organisms by this method, especially the Gonococci, stain a brilliant red and pus cells greenish-blue. The Gonococci are found in regular clumps of Diplococci, the distance between each pair being much the same. Some are intracellular.

(Pyronines are derivatives of diphenylmethane. Pyronine "G" is used. On oxidising Pyronine "G" Acridine Red is obtained.)

The diplococcus can usually be readily found in large numbers in discharges of gonorrhoeal origin, but a diplococcus of similar appearance is also apparently to be found not infrequently in vaginal discharge of non-gonococcal origin. If a distinction is to be made it is best to try to grow the organism in question on the ordinary forms of culture media, as, while the gonococcus will not grow on plain agar, it grows freely on blood agar. On the other hand, the other forms of diplococcus met with in the vagina usually grow freely on plain agar. It is also possible that the presence of the diplococcus inside the pus cell is characteristic of the gonococcus, but one must be a trained microscopist, who is continually examining such preparations, to be certain that what appears to be inside the cell is not really lying directly below or above it. Therefore, in cases in which a diagnosis is of serious importance, it should never be based on a mere clinical examination.—J. E. R. McDonagh.

Acid Thionin.—Thionin 0.5%, Glacial Acetic Acid 5% in Distilled Water stain 3 minutes, wash in tap water. A very reliable stain,—shows phagocytosis well and the characteristic "kidney" shape of the Cocci. Best stain for general use when confirmed by 'Gram.'—Wyatt Wingrave.

(Thionin $C_{12}H_8N_2S$ can be made from para-phenylenediamine by oxidation in the presence of H_2S .)

Jenner's Stain, q.v., also gives excellent results.

Nissl's Stain.—Methylene Blue, 'B Patent,' 3.75, Soft Soap 1.75, Water 1,000. Stain thin smears (fixed in air) without heating, for 1 minute, wash, blot and examine.

Other Diplococci:—*D. albicans amplius* Bumm, found in mucus in the healthy vagina; *D. albicans tardissimus* morph. identical with the *Gonococcus*; *D. Coryzae*, *D. intracellularis Meningitidis* (v. Cerebro-spinal Fever), *D. of*

orchitis found in gonorrhœal pus during the first two days pathogenic), *D. pneumoniæ*, *syn. pneumococcus* of Frankel, *q.v.*, *D. pyogenes ureæ*, and *D. Catarrhalis*, *vide M. Catarrhalis*.

N.B.—*Pneumococcus* is the only Gram + Diplococcus. Capsule well marked in pus, but not in culture. Cocci, elongated or lanceolate, converts oxy- into hæmoglobin in the culture. Will not grow on Gelatin.

Complement Fixation.

As a result of a year's experience in using the test in women it is thought not sufficiently powerful to diagnose the disease; in the middle stages it will differentiate between gonococcal and non-gonococcal disease; and in the convalescent stage it is too delicate for use as a practical sign of cure.—J. J. Abraham, L. i./24,431. *Further refs. Vol. II., Edn. XVIII, p. 524.*

Vaccine Therapy.—See Vol. I.

Guinea Worm. *DRACUNCULUS MEDINENSIS*, *Syn. D. Persarum, Filaria Dracunculus, F. Medinensis*.

Found in parts of India (Deccan, Scinde, etc.) in Tropical Africa, Persian Turkestan, Arabia, especially on West Coast of Africa. In parts of the latter nearly every negro has one or more specimens about him. The size of the female parasite is about $1\frac{1}{2}$ mm. by 90 cm. as average. Its habitat is the connective tissue of the limbs and trunk. It has been thought the infection of man occurs by ingestion of infected cyclops as 0.2% Hydrochloric Acid arouses the larvæ in an infected crustacean while the latter are killed. Evidence is fairly complete as to this mode of infection, but it must not be supposed that every species of cyclops can act as intermediary host. Leiper fed monkeys on bananas containing the infected Cyclops and at the autopsy six months later obtained both male and female forms. As to **treatment**, see Vol. I. p. 1065.

Hog Cholera.—*B. Suipestifer* (or *Bacillus Aertryck*) was isolated from cases of hog cholera, although the infection is now known to be due to a filterable virus. It has been found in the intestine of normal pigs, and may originate meat poisoning, especially where pork is the substance at fault. It shows close resemblance to *B. para-typhosus* "B" and to demonstrate it the method of absorption or complement fixation must be employed. It belongs to the Gärtner Group, see *B. Enteritidis*.

Paisley outbreak of food poisoning was due to milk containing *B. Aertrycke*.—W. R. Wiseman, B.M.J. ii./22,728.

B. Suipestifer (or *aertrycke*) type mutton food poisoning.—W. Allen Young and G. D. Dawson, L. ii./22,608. See also *ibid* 609.

Loch Maree Hotel food poisoning tragedy (1922). Eight persons lost their lives through eating wild-duck paste. The shortest incubation period was 14 hours and the longest 43 hours. *B. botulinus* and its toxin was found in one of the pots of paste.—T. K. Monro and W. W. N. Knox, B.M.J. i./23,279.

Fatal case due to eating pork, infected by *B. Suipestifer* *B.* The bacillus may also be found in mutton and beef. The disease varies in severity, fatal results being uncommon.—B.M.J. ii./24,857.

See also Food Poisoning, under Botulism.

Bacillus Influenzæ, *Syn. PFEIFFER'S BACILLUS*. A very small bacillus non-motile. Does not stain by Gram's method, nor grow on ordinary media unless hæmoglobin be present.

Cultivation.

B. Influenzæ grows best on a moist Hæmoglobin Agar containing no Glucose—in many respects opposite to the gonococcus in cultivation requirements.—D. Thomson, L. i./19,1106.

Blood Agar made by boiling the agar medium with blood for a minute and separating the coagulated protein is a good medium for growing *B. Influenzæ*. Or Blood 1 Cc. may be diluted with 9 Cc. of water and boiled. The clear liquid added to Nutrient Agar is also an excellent medium for the organism, or strong mineral acids, *e.g.* Sulphuric, may be used without heat to act upon blood and the liquid subsequently neutralised with Soda.—A. Fleming, L. ii./19,138.

Blood digested by Trypsin as medium for growing Influenza B.—J. Matthews L. ii./18,104.

Paul Fildes' Medium.

Mix in the following order N. Saline solution 150 Cc., pure Hydrochloric Acid 6 Cc., Defibrinated Sheep's Blood 50 Cc., and Pepsin B.P., 1 Gm. Shake to dissolve and place in water-bath at 55° C. for 2 to 3 days. Adjust the reaction to pH=7.6 by adding 20% Sodium Hydroxide solution 12 Cc. or more until a permanganate colour is produced with Cresol Red. Now add Hydrochloric Acid drop by drop until Cresol Red gives practically no change in colour but Phenol Red gives red (pH=7.0 to 7.2). Finally add 0.25% Chloroform. For use, add the medium directly to melted Agar at 60° C. in a strength of 2 to 5%, or to broth in the same proportion. It is not necessary to remove the Chloroform. The correct adjustment of the reaction is important. The pneumococcus occurs very frequently in conjunction with the influenza bacillus. A mixed flora in the secretions in these cases is characteristic. Influenza bacilli are commonly found in the throat in pertussis, measles, and pulmonary tuberculosis. *cf. Vol. I., p. 921.*

Vaccine Therapy is fully dealt with in *Vol. I., p. 921 et seq.*

Pfeiffer's organism causal of influenza in certain troops but not in others.—J. W. Edington, *L. ii./20,340.*

Periodicity of Influenza. Evidence pointing to the existence in this country of a minor cycle of 33 weeks and in addition a major cycle round about 10 years maxima.—J. Brownlee, *L. ii./19,356*; C. O. Stallybras, *L. i./20,372*; see also B. E. Spear, *ibid*, 589.

Influenzal pneumonia. Hydrogen Peroxide transfusion 2 ozs. of "10 vol." in 8 ozs. of Normal Saline. Gas embolism is not produced. Anoxæmia often markedly benefited. Toxæmia overcome in many cases.—T. H. Oliver & D. V. Murphy, *L. i./20,462.*

Distemper in Dogs.—The M.R.C. has been studying this affection. There is good reason to think it offers a close parallel to human influenza.

A search for a **serum** is being made at Mill Hill under the auspices of the "Field." Certain unofficial sera are on the market. There are three varieties of distemper—head, chest, and abdominal—the head being the most serious, as in this the virus has attacked the central nervous system and it is likely to lead to chorea. Sudden and unexpected nervous or paralytic seizures are seen. Infection may possibly depend on nutrition and condition of the dog. For the present, diet, and small frequent doses of Quinine Salicylate are advised.—C.D. *ii./26,462.*

Researches by P. P. Laidlaw, also at Mill Hill, under the direction of the M.R.C., suggest the possibility of immunising dogs against the disease. He has inoculated a pure-bred puppy with distemper virus and under the new treatment it recovered with only a few hours' rise in temperature of no importance.—P.J. *i./27,16.* A vaccine of value—*L. ii./28,1250.*

Caused by a filter-passing virus, which abolishes the natural or acquired resistance to pathogenic bacteria. Immunity can be produced by injecting 10 Cc., of a preparation obtained by removing the spleen from an animal killed during the height of the febrile stage of the attack, crushing this organ and emulsifying 1 in 10 in normal saline. The virus is killed by adding an antiseptic, preferably Formaldehyde, and after 48 hours it is ready for use.—J. Lebailly, *Comptes Rend.*, 1927, 185, 370, per P.J. *ii./27,527.*

Johne's Disease in cattle due to *Mycobacterium bovis*, an acid fast bacillus which is distinct from the tubercle bacillus. F. W. Twort grew the organism on the special culture medium used by him. Vaccines for the diagnosis of Johne's disease in cattle as distinct from tuberculosis may possibly be made. Communication to Royal Society of Medicine, Nov. 1, 1910; *Nature*, Nov. 24/10, 127.

Leishmaniasis.

Leishmania parasites give rise to several diseases:

Kala-Azar.

Occurs in India, China, S. Russia, Mesopotamia, the Mediterranean littoral, the Blue Nile, and in Kenya Colony, and is a disease of children or young adults. Left untreated it nearly always ends fatally in a few months in acute cases, or in a few years in chronic cases. There seems no reason to separate the Mediterranean leishmania from that of India, and the parasite of kala-azar wherever it occurs may be designated *L. donovani*. Diagnosis is established by discovery of its parasite, by making films of material obtained by puncture

of the spleen (or of the liver, which is less dangerous) and staining by Romanovsky stain. It is generally assumed that *L. donovani* has an invertebrate host e.g., bugs or fleas, but the problem still remains unsolved.

Oriental Sore, Syn. Tropical Ulcer, Delhi Boil, also (in the New World), **Espundia**, Uta, Buba, Pian-bois, Forest Yaws, and Bosch Yaws.

Oriental Sore is widely distributed: it occurs in Spain, Italy, Greece, France (one case), N. Africa, Egypt and the Sudan, Asia Minor, Arabia, Mesopotamia, Persia, S. Russia, India and S. America. The disease in the New World seems to be more severe and of longer duration than in the Old World, and the parasites causing the two diseases may not be identical, but it seems better to retain the name *L. tropica* for both forms until more reliable proof of difference is forthcoming.—Wenyon.

In addition to "*espundia*," in Brazil, there is a further Leishmania infection introduced from the Eastern Mediterranean, known as "*Aleppo bouton*," a systemic disease.—H. R. Carter, Int. Conf. Trop. Am., '24, 483.

The oval "**Leishman-Donovan**" bodies ($2.5 \times 3\mu$) are present in every case of Kala-Azar and are the cause of this deadly disease which is by no means confined to India. Sir L. Rogers in 1904 found that if kept in a sodium citrate solution at about 22°C . these bodies undergo multiplication, showing that they are capable of living outside the human body in some cold blooded animal, possibly an insect, but the life history remains to be completed. Similar parasites have been found in Oriental Sore and more recently in a variety of other ulcerative affections in tropical America and in the Sudan, one of them—*espundia*—being a very grave disease.—Sir Patrick Manson, B.M.J. ii./17, 105.

Noguchi has shown that the Leishmanias found in dermal conditions are different from the Leishmania of kala-azar, and the old theory that Oriental Sore is merely a manifestation of kala-azar is entirely disproved.—A. Castellani, Int. Conf. Trop. Am., '24, 479.

Cultivation.

Leishmania donovani, *L. infantum*, *L. tropica* and *L. brasiliensis* grow well on semi-fluid agar medium and form heavy greyish surface growth several mm. in depth. All the strains require Oxygen for growth and none grow in atmosphere of Hydrogen, Nitrogen or Carbon Dioxide. Distilled water caused immediate disintegration of flagellates, while tonicity greater than 0.3% and up to 0.9% Sodium Chloride is well borne. Organisms immobilised by half saturated saline solution. Saponin in 1:10,000 dilution killed cultures without dissolution of bodies or flagella. Ricin 1:1,000 caused immobilisation and agglutination. *L. donovani*, *L. tropica* and *L. brasiliensis* each represent a serologically independent and distinct unit. *L. infantum* serologically identical with, or closely allied to, *L. donovani*. These findings conform with clinical observations which indicate that visceral leishmaniasis (*L. donovani* and *L. infantum*) are distinct from benign Oriental Sore (*L. tropica*) and probably also from the American type of leishmaniasis (*L. brasiliensis*).—H. Noguchi, Int. Conf. Trop. Am., '24, 466.

The life-cycle of kala-azar.—L. ii./26, 506.

The bed-bug and the common louse exonerated from transmission of kala-azar. "For the present the sand-fly (*Phlebotomus argentipes*) must be held to be the probable transmitter." The parasite of kala-azar should be known as *Herpetomonas donovani*. Report of kala-azar Commission in India.—L. ii./26, 140.

Though final proof of experimental transmission has not yet been obtained there is very good circumstantial evidence that the sand-fly is the actual vector of kala-azar and Oriental Sore.—C. M. Wenyon, B.M.J. ii./28, 208, 558. This view was supported by E. Hindle and other speakers, *ibid*.

Kala-azar in soldiers returning from Malta. Spleen puncture will show evidence of large numbers of typical parasites. Diagnostic methods—diarrhoea and splenomegaly. The latter is not so marked in enteric as in kala-azar and is not so solid to the feel.—G. R. Ward, L. ii./16, 16.

Kala-Azar in Mesopotamia, discussion as to.—J. C. G. Ledingham, B.M.J. ii./19, 88, 667; see also G. C. Low, *ibid*. 758.

X-rays in oriental sore.—L. ii./20, 893.

In a well-established case, the serum sets immediately, like the white of an egg. There is marked leucopenia and a great reduction in proportion of white to red corpuscles. By careful examination of blood films, the parasite can

found in the peripheral blood in nearly 100% of cases.—Napier and Muir, B.M.J. ii./23,719-720.

The aetiology of Kala-azar and tropical sore.—B. Blacklock, L. ii./23,273. Phlebotomus flies believed to transmit to man the Three Day Fever and Oriental Sore.—M. Neveu-Lemaire, Jl. Trop. Med., Feb. 1/23,46. See also de C. Cerqueira, per Jl. Trop. Med., June 1/23,199.

Immunity to Oriental Sore.—The natives of the Turkestan and the Caucasus develop a natural immunity and new arrivals to the district are always more apt to become infected than the settlers. Complete immunity can be brought about by an experimental sore, but only when it is allowed to develop and heal naturally. Preventive inoculation on covered parts of the body can be recommended, if care is taken to avoid sepsis or inoculation with syphilis.—E. I. Marzinowsky and A. Schurenkova, Trans. Roy. Soc. Trop. Med., Vol. 18, No. 1, May '24, p. 67.

Test for kala-azar.—Add 2 Cc. of patient's blood, taken from one of the ante-cubital veins, to a solution of 0.1 Gm. Urea-Stibamine in 3 Cc. distilled water. In positive cases a thick, white, curdy, precipitate appears almost instantly.—I.M.G., Dec., '27, per Jl. Trop. Med., Apl. 2/28,87.

Leprosy.

The Chaulmoogra Treatment is in Vol. I., p. 606: Leprosy as a self-healing disease, ibid. p. 612, also this chapter, p. 555: Vaccine treatment, Vol. I., p. 613: see also Therapeutic Index, p. 1073.

The presence of *B. lepræ* (*Hansen's Bacillus*), the specific organism of leprosy in the mosquito (*Culex pungens*) and in the bed bug (*Cimex lectularia*) has been shown.

Etiology.—A friend of the writer in Brazil, who has travelled there for scientific research (though not a medical man) has written at frequent intervals on the subject of the spread of the disease. In the Preface of the 18th Edition a lengthy account of his views was printed. He held that the spread of leprosy in S. America has a definite relation to the bugs and mosquitoes, but so far as Brazil is concerned the former could not be blamed, because for some unexplained reason bed-bugs do not exist in the Amazonian villages. (Feeding experiments with bugs fed upon nodules, in Liverpool and in Panama, were entirely negative.—D. Thomson, B.M.J. ii./13,849. But an exactly opposite result was described by Long in 1911.) He seems far more inclined to blame mosquitoes.

Later he wrote us as follows:—

"I think, perhaps, I ought to lay more emphasis on the fact that whatever has led me to suspect the instrumentality of the mosquito in the spread of the disease does not lessen my suspicions of other biting insects. On the contrary, whatever appears to implicate the mosquito would, by analogy, lead me to suspect other blood-sucking parasites, especially those habitually associated with the abodes of man.

"It would be superfluous here to go into the significance of the distribution of leprosy, and its ready demonstration of the occurrence of leprosy, and its propagation, independent of mosquitoes. It would be more to the point to suggest that the attention of leprologists might profitably determine whether the disease is being steadily propagated anywhere, locally or regionally, in the undoubtable absence of blood-sucking, parasitic insects, to furnish the hypothesis of an insect agency. Conversely, in places where leprosy has been introduced, and has failed to spread, it would help towards shaping our opinion to know whether this failure to propagate itself has been coincidental with an absence of any, or all, of the suspected parasites, and which of these, if any, were present.

"A study of the literature on the subject leaves no doubt that opportunities for research on these lines have been thrown away, and even by some of the specialists who we might expect to lead us out of the darkness which still enshrouds the etiology of the disease."

Mode of transmission.—Some interesting experiments showed that flies, mosquitoes and other insects spread it, but in particular *Acanthia lectularia* appears to constitute a very important agent in the spread. Acid-fast bacilli resembling *B. lepræ* have been found in 30% of specimens up to 10 days after feeding on lepers.—T. Lindsay Sandes.—B.M.J. ii./11,469.

Love of the leper for fish diet, generally in a state of decomposition.—B.M.J. i./11,1234.

Hereditary transmission of predisposition difficult to prove. Of 398 children of leprous parents, 231 were non-leprous and no case of congenital leprosy was observed.—per. Pres., June, '28,211.

Distribution.—Equatorial Africa has a higher incidence of leprosy than any other region in the world, the rate being as high as 130 per 1,000 in the Ebolawa District. The total number of lepers in China is estimated at 1,000,000; in 1912 Japan had 102,000 lepers, and in 1921 India had about the same number. Chinese immigrants seem to have been an important factor in the spread of leprosy. Every country with a high leprosy incidence is within the tropics, and practically all of them have a high rainfall, the disease being nearly or completely absent from those parts in which the rainfall is less than 10 inches.—A review of "Leprosy" (Rogers and Muir), J. A.M.A. ii./25,381.

High rainfall and humidity increase the incidence in large areas in India and poverty of diet and consumption of decomposed fish are predisposing factors.—per Pres., June, '28,211.

Contact cases of leprosy in the British Isles.—J. M. H. MacLeod, B.M.J. i./25,107.

Leprosy essentially a disease of the unhealthy—little chance of arresting disease unless predisposing causes, *e.g.*, syphilis, malaria, etc., are dealt with. It is now an established fact that **only about 3% of lepers actually die of leprosy**. Many lepers cannot be helped much because the anæsthesia and other signs of nerve lesions are often result of nerve destruction, the leprosy having died out.—R. G. Cochrane, L. ii./26,95.

In China leprosy seems to be specially associated with water-logged and ill-drained areas. But for the aid rendered by the Christian Church the lot of the leper in China to-day would be hopeless. Modern scientific methods coupled with a voluntary form of segregation on the part of the lepers themselves, give good prospects of changing the entire outlook of China's lepers and ultimately of ridding China of leprosy.—China Med. Jl., per Jl. A.M.A. ii./25,931.

Since the establishment of segregation in Norway in 1856, leprosy has become increasingly rare, though previously it was decidedly on the increase.—Sir A. Newsholme, Int. Conf. Trop. Am., '24,791.

Spread, mode of infection and prophylaxis of leprosy. The incubation period is 2 to 8 years or more. One fifth of recorded cases were through conjugal relationship or cohabitation with a leper. Inoculation is probably through an accidental abrasion in skin or mucous membrane. This theory satisfies many findings.—Sir L. Rogers, L. ii./22,17; see also B.M.J. i./22,98.

Incubation Period.—An analysis of 84 cases recorded shows that the disease developed in within less than 5 years after exposure to infection in 92% of them. The average period between exposure to infection and the development of the disease was 2 years and 2 months. There is a direct relationship between the closeness of contact with the disease and the early development of symptoms, the incubation period of a few cases of direct inoculation being under two years and usually about 6 months.—Sir L. Rogers, Ind. Med. Gaz., Feb., '24, per Jl. Trop. Med., Mar. 15/24,72.

Diagnosis.

Bacillus Lepre has morphology similar to *B. tuberculosis*, but usually occurs more in clumps and is said to be tapered at the ends. Stain irregularly, and are more readily decolourised than *B. tuberculosis* by inorganic acids.

Obtain material from a nodule and stain the smear by 'Ziehl-Neelsen' using 20% Sulphuric Acid or by 'Gram' counterstaining with Bismarck Brown. The organisms (Gram +). Finding *B. Lepre* in nodules is usually easy, but it is extremely difficult to find in the spots of nerve leprosy; the nasal mucus should be examined, after giving a large dose (60 grains) of Potassium Iodide. The following features distinguish them from the *Tuberculi bacilli*; they occur grouped together in huge numbers, stain more solidly and granules when present are coarser than those of *T.B.* and are decolorised more easily. Certain cultivation or inoculation into experimental animals with pathogenic results is not possible.—Stitt.

Cultivation of *B. Lepræ*.

Kedrowsky claimed to have cultivated the leprosy bacillus. Examination of his organism showed there was **not evidence that his acid fast bacillus was that of leprosy.**—H. Fraser & W. Fletcher, L. ii./15,13.

The most favourable medium for growth appears to be either Placental-Extract-Agar or Horse Serum Nutrose-Agar with the addition of 2% ground-up *Smegma Bacilli*. Kedrowsky's work on the variable morphology and staining properties of the *Lepra Bacillus* is confirmed. Agglutination, precipitation, complement-deviation and percutaneous tests can be used to prove the relationship of acid-fast or other germs cultured from cases of leprosy. Rat and human leprosy appear to be identical diseases. It is therefore possible that the germ of both can be transmitted from one to the other, given an appropriate intermediary.—Bayon, B.M.J. ii./11,1269; L. ii./11,460.

The organisms isolated from the lesion of human leprosy.—C. Duval, B.M.J. ii./12,1189. Problem of leprosy, M. E. Marchoux, *ibid.* 1191. Study of various cultures of *B. Lepræ*.—H. Bayon, *ibid.* 1191. See also L. ii./12,1791.

The leprosy bacilli, in live tissues or laboratory media, may be both acid-fast and non-acid-fast. In pure cultures, acid-fast microbes are received only in exclusive cases. In most cases diphtheroids develop, with either very much lowered acid-fastness or none at all. The leprosy bacillus should be placed in the group of actinomyces or streptothrices-like microbes and the bacillary form represents only one of the forms of its state of being.—W. J. Kedrowsky, Jl. Trop. Med., Jan. 16/28,21.

Of 157 deaths at Makojai Leper Hospital, 42 were due to tuberculosis and only 14 to leprosy.—Jl. Trop. Med., July, 1/22,216.

Transmission of leprosy from rat to man.

In a case of leprosy at the Pasteur Hospital there were numerous scars resulting from the slow healing of ulcers, and when their surface, or the nasal mucous membrane, was slightly scraped and the substance obtained examined under the microscope, numerous fine, short, cocciform bacilli were seen, to which Prof. Manchoux provisionally gave the name *Mycobacterium pulviforme*. After death, great quantities of these were found in the skin, lymph glands, liver and spleen. As a result of inoculation from this spleen, 5 out of 7 rats contracted a disease practically identical with rat leprosy. The relation of rat leprosy to human leprosy may be similar to that of bovine to human tuberculosis. 0.6% of Parisian sewer rats are definitely leprosy.—L. ii./23,1309.

Complement-fixation Test for leprosy.—Pres., Nov., '24,390.

In 24 cases of leprosy the Wassermann test was positive; only one case was doubtful.—Per Jl. Trop. Med., Sept. 15, '25,344.

"**Victoria Blue**," as a stain for *B. Lepræ* (Mühlpfordt), has a definite affinity for lipoids and hence for spirochetes. Schilmacher's modification is: Victoria Blue (2 parts) dissolved in 50% Alcohol, mixed with equal quantity of 4% solution of Carbolic Acid, to which is added 10% aqueous solution of Glycerin. The smear containing spirochetes is fixed with Alcohol, the solution poured over the slide and heated for 15 seconds.—B.M.J. E. i./25,14.

The British Empire has more known lepers than any other political entity in the world, but is doing far less in proportion than is being done by the United States for its lepers. Only a small proportion receiving Chaulmoogra treatment.—British Empire Leprosy Relief Association, B.M.J. ii./23,118.

Treatment.—The important advance made in the treatment of Leprosy in India is the adoption of **Potassium Iodide**. Clinical and pathological study at the Calcutta School has led to classification of certain types and phases of leprosy which benefit from Iodide. (Report of the Indian Council of the B.E. Leprosy Relief Assn.).—L. ii./28,472.

A thorough disinfection of the nose is one of the first essentials in treatment. A solution of **Ammonium Persulphate** 3.7% and Hydrochloric Acid 1% in water has been used. Inhalation of the fumes of **burning sulphur** has also been employed.

Vaccine Treatment it is claimed has been successful. See Vol. I., p. 613. Earlier Refs. in general, Vol. II., 18th Edn., pp. 528, 529.

Leprosy: a self-healing disease.

The natural and **increased production of lipase**, or fat-splitting ferment in the blood and tissues is an important factor in the protective processes or induced resistance of the body, which offers a reasonable

explanation of the **therapeutic effect of Sodium Morrhuate** and, in part, of **Sodium Chaulmoograte, both of which increase the action of lipase in vitro.**—J. A. Shaw-Mackenzie, L. i./24,518. The *blood lipase* in turn dissolves the fatty coating of the leprosy bacillus (and the tubercle bacillus).—Sir L. Rogers, B.M.J. ii./23,11.

The normal course of leprosy is that of a self-healing disease, like small-pox, enteric and other diseases, but whilst enteric completes its course in, say, 21 days, leprosy may take 21 years to burn itself out. Most of the treatments of leprosy which have had any vogue owe a great part of their successes to the fact that leprosy tends to get better spontaneously and hopeful suggestion helps the tendency to cure. It is criminal to assert that leprosy is not amenable to treatment, though perhaps equally wrong to claim that there is a specific cure. Leprosy is a disease which can be benefited by treatment, the majority of early cases having a fair chance of losing all signs for the rest of their lives, providing their general health is maintained. The infectiousness is exaggerated. In any country in which the incidence of the disease remains the same over a long period of years, each victim, on the average, communicates the disease to one other person.—Leader, I.M.G., June, '24/299.

Pre-disposing causes.—E. Muir, L. i./25,169. See also this authority on *Self-healing*, Vol. I., p. 612-613.

LEPROSY IN INDIA.

15% of general skin out-patients in the Skin Diseases Clinic of the Calcutta School of Tropical Medicine are early and undiagnosed cases of leprosy. Evidence points to inoculation as method of transmission. Those living in contact with infectious cases get lepra bacilli on their skins, a scratch or lesion implanting the bacilli under the skin; there is always, if looked for, a heraldic lesion. The natural tendency is towards recovery, which can be hastened by Chaulmoogra with suitable diet, etc., a cure resulting, in many cases, within a period measurable by months. The mutilated, anæsthetic cases are not infectious but the early, nodular cases, unsuspected and undiagnosed are. They should be segregated in preference.—I.M.G., July /24,354.

Liver Abscess. A form of suppuration of the liver occurring in warm climates, principally in male Europeans and in association with amœbic dysentery. (*E. histolytica* infection.) Drainage, dressing and emetine hypodermically requisite.—A. L. Candler, L. i./20,429. See DYSENTERY.

Malaria.

Quinine Treatment:

For the Quinine Treatment of Malaria see Vol. I., p. 743. For Cinchonine see Vol. I., pp. 724,744. Quinidine and Cinchonidine, 719, 723. See also *Therapeutic Index*, Vol. I., p. 1075.

To **prevent the spread of Malaria** it is customary to improve surface drainage and so obviate breeding places of the larva of the mosquito. Wire gauze, netting and the like are employed as protectives to man.

Antilarval measures.—Common Kerosene poured on the surface of pools, lakes, etc., is useful. It forms a scum which prevents the larvæ from breathing and hence kills them. See also First Internat. Congress, B.M.J. ii./25,970.

Thirty pounds of oil will cover at least 2,000 square yards of water; the dose of paraffin should be repeated about 20 times during the year.

"**Bamber Oil.**" Citronella Oil (not lemon grass oil) 1½, Kerosene (Paraffin) Oil 1, Cocoa Nut Oil 2, to which is added 1% Carbolic Acid. As a preventive against malaria instead of the mosquito net. Its efficacy lasts 4 to 6 hours—sufficient for a night's sleep when a net is not available.—C. Christy, L. ii./17,482.

Rice cultivation with the necessary stagnant water is no small source of increase of malarial disease.

Paraform recommended for destruction of anophelinæ larvæ, 0.25 Gm. (mixed with chalk 0.08 Gm. in calm weather, or sand 20 Gm. in windy weather) is used for each square metre of surface.—Roubaud, T.D.B., Vol. 17, 1921/115.

Smoke production as a measure of mosquito control.—J. M. Shapiro, per JI. Trop. Med., Feb. 15/23,46.

The use of gases and vapours for killing mosquitoes breeding in wells.—K. B. Williamson, Trans. Roy. Soc. Trop. Med. Vol. 17, No. 8, Feb., '24, p. 485.

A few drops of Carbon Bisulphide poured into a 10-gallon tub, the water of which was swarming with the larvæ of mosquitoes, killed them all in half an hour, without affecting the water either in taste or smell.—A. K. Fisher, *Jl. Trop. Med.*, Nov. 15/23, 340.

Insects and War. The mosquito—means of prevention and description.—A. E. Shipley, *B.M.J. i./15*, 797.

Egyptian Expeditionary Force, Malaria in, during 3½ years. Epidemiology, microscopy, etc., concerning (1) Egypt and the Canal Zone, and (2) Palestine, Caused by 2 species of parasite—the benign tertian and the malignant or subtertian. The quartan appears to be almost non-existent in Egypt and to occur rarely in Palestine.

The main mosquito intermediary in the benign tertian zone in Palestine appears to be the spot wing (*A. Maculipennis*) and in the Jordan Valley *A. Palestinensis*.—P. Manson-Bahr, *L. i./20*, 79.

Excellent résumé of advice for soldiers and others on prevention of malaria.—C. Christy, *L. ii./17*, 485.

Histology of cases rapidly fatal in the Salonica force in 1916. Examinations of brain, heart, muscle, adrenal glands, kidney, liver, etc.—L. S. Dudgeon and C. Clarke, *L. ii./17*, 153.

Incidence of malaria among our troops in Macedonia, Mesopotamia and East Africa.—*B.M.J. i./18*, 350.

Malaria, 12,000 cases in Macedonia treated by A. C. Alport (Review).—*B.M.J. ii./19*, 467. Thyroid gland enlargement in malaria.—J. B. Hume, *B.J.M. ii./19*, 661.

Localisation of malarial parasites in man.—W. M. James, *Int. Conf. Trop. Am.*, '24, 67.

Classification of American Anopheline mosquitoes and their relation to the transmission of malaria.—F. M. Root, *Int. Conf. Trop. Am.*, '24, 148–156.

The cost of malaria control.—J. A. Le Prince, *Int. Conf. Trop. Am.*, '24, 157–164.

The Northern provinces of Argentina are markedly infected with malaria.—P. Mühlens, *Int. Conf. Trop. An.*, '24, 552.

Larvicides in mosquito control, using White Cross *Cresylic Disinfectant*.—J. F. Marshall, *L. i./25*, 1380.

Some aspects of malaria control.—W. E. Deeks, *Jl. Trop. Med.*, July 1, '26, 185–194.

Subtle chemical differences (alkalinity or acidity) in breeding waters may be a factor in determining species of larvæ found in them.—*Inst. Med. Res. of Federated Malay States*.—*B.M.J. i./26*, 1053.

Etiology.—There exist sexual (sporogony in the mosquito) and non-sexual (schizogony in man) cycles of the parasite. Various workers, notably Grassi and others have observed the complete development of the malignant parasite in *Anopheles Claviger* and the partial development of the tertian parasite in the same anopheline. (For a Historical Account see Wenyon, Vol. II., p. 909.)

Man is the only malaria-carrier. Any person infected with malaria, irrespective of number of parasites present, may become an effective carrier and a source of infection. The malaria-carrier bears a direct relation to malaria prevalence.—C. C. Bass, *Int. Conf. Trop. Am.*, '24, 61.

Malarial Parasites.—The mosquito theory of this disease was established by Sir Ronald Ross (the winner of the 1902 Nobel Prize) after Sir Patrick Manson (1894) and others had paved the way.

Transmission of malaria. Pfeiffer's hypothesis (1892), said to be the most accurately deduced of those hitherto put forward. Parasite, according to him, may have a life cycle similar to the common coccidium of the rabbit, completing itself in the body of some blood-sucking invertebrate, which might inoculate the germs thus produced into human beings. There is close relationship between malarial parasites and coccidia.—C. M. Wenyon, *L. ii./23*, 68.

Classification of the Malarial Parasites.

That adopted by Manson in his "Tropical Medicine" was given briefly in our last and previous editions.

The nomenclature and views on this classification have been subject to frequent modification.

Briefly—there are, it is agreed, three *species* of the malarial parasite (a) *Plasmodium vivax* of **Benign Tertian** with a cycle of 48 hours (b) *P. malariae* of **Quartan** malaria with a cycle of 72 hours (c) *P. falciparum* of **Aestivo-Autumnal** or **Malignant Tertian** with cycle of 48 hours.

The mosquito-malaria theory was formulated by Sir P. Manson in 1894. From the fact that the flagellated body does not come into existence until the blood has left the blood vessels—that is until it is outside the body—he concluded that the function of the flagellum lay outside the body—in fact that the flagellated body was the first phase of the extracorporeal life. As the parasite while in the circulation is always enclosed in a blood corpuscle and therefore unable to leave the body of its own efforts its removal must be effected by some blood sucker. The mosquito was correctly suspected. Sir Ronald Ross proved finally in 1898 the extracorporeal phase of the parasite.

Mosquito-malaria theory. A good summary of the proof of the theory commencing with the discovery of the parasite by Laveran in 1880.—Sir Patrick Manson, B.M.J. ii./17,103. See also R. McCarrison, *ibid* 109.

It has been computed that $\frac{1}{4}$ billion parasites must be present to produce fever, but in an experimental “inoculation” not one parasite could be found in the blood during the first three days of fever, while during the last three days as the fever subsided parasites were found.—M. D. O’Connell, L. i./20,518.

Key to Anopheline species of India, Ceylon, and Malaya. Of benefit to the Tropical practitioner. An outstanding example of simplicity, conciseness and accuracy—19 pp. by Prof. Strickland—review.—B.M.J. ii./25,851.

Staining Methods.

Films of blood smeared evenly with a very small quantity, *s.a.*, dried in the air, not by aid of a flame, and fixed by immersing in alcohol and ether, equal parts, 10 minutes, may be stained with aqueous methylene blue and eosin, or with methylene blue alone, 5 minutes, or with a Hæmatoxylin Stain, or by **Leishman’s Stain** (*q.v.*). With Leishman’s Stain fixing is not necessary. **Muir** says the structure of the parasites is well brought out by the following—Soak film in Saturated Corrosive Sublimate Solution a few seconds. Wash well, stain with hæmalum 10 minutes, wash, stain again for about the same time with aqueous methylene blue. Wash in water, dehydrate, clear in Xylol and mount in balsam. The chromatin of the parasites is violet blue, and the protoplasm pure blue. The Leishman method is, however, principally in use. Consult Allbutt’s *System of Medicine*, or M. & R.

Leishman’s Stain made by dissolving 1 Gm. of the powder in 200 Cc. Methyl-Alcohol and 12 drops 1% NaOH added. Used for general purposes. In staining, stain for 30 seconds with this then dilute with distilled water about 1 in 4 for a further 2 to 3 minutes. Wash with distilled water and drain. **Gauducheau’s Stain** used when Leishman’s fails.—P. Manson-Bahr, L. i./20,79.

Gauducheau’s Stain has the following composition:—

Borrel’s Blue	6 Cc.
1% Methylene Blue in 90% Alcohol	18 Cc.
0.5% Water-Soluble Eosin (blue shade) in Absolute Alcohol	30 Cc.
Absolute Alcohol	140 Cc.

In use, apply the stain, undiluted, to the film, leaving it on about one minute. Then dilute with four parts of Distilled Water (*neutral*). Each batch of stain requires a different length of time for standing. New stain requires about half an hour, old stain about 20 minutes. In the East, 20 minutes for new stain and 7 minutes for old stain were found amply sufficient, but in England it takes longer.

Borrel’s Blue may be made as follows:—

Dissolve a small handful of Silver Nitrate crystals in hot Distilled Water in a 100 Cc. flask. Fill up with 10% Caustic Potash Solution. Wash the resulting precipitate of Silver Oxide about 12 times in boiling Distilled Water, then fill up the flask with saturated aqueous solution of medicinal Methylene Blue. Plug the flask loosely with cotton wool and place in direct sunlight for a day or two (it prevents subsequent precipitation when the stain is exposed to light during later use). Then cork, place in the incubator

t 37°C. for one month, removing cork and shaking occasionally. Filter at end of month; the filtrate = Borrel's Blue. Details kindly supplied by J. Graham Willmore.

Some modifications in the thick-film method in the examination of blood from malaria parasites.—M. A. Barber and W. H. W. Komp, *Int. Cont. Trop. Am.*, 24, 110.

Manson's Method for demonstrating Flagellate bodies in Malaria.

Blood films are dried and fixed in absolute alcohol (5 minutes). Haemoglobin is washed out by dropping on 15% Acetic Acid. The film is then washed in water and stained for 6 hours or longer in 20% Carbol Fuchsin. It is then washed, dried and mounted as usual.—*Essentials of Practical Bacteriology*, I. J. Curtis.

Cultivation of the malarial parasite in vitro. 51 cases.
—L. S. Dudgeon and C. Clarke, *L. i.* 17, 530.

General Paralysis Treatment of, by inoculating malaria
—See p. 1080, Vol. I.

Malignant Oedema. *Bacillus Oedematis Maligni*, Koch. *Syn.*
Bacillus Oedematis, *Vibron Septique* of Pasteur.

Obtained from surface garden soil, dung, dust, putrifying matter, etc. Anaerobic—Single rods 3 to 10 μ in length frequently in cultures in long filaments. Stains Gram—, in this differing from *Bacillus Anthracis*. Gas forming. Liquefies gelatin. Spores very resistant—may be kept for months in the dry condition.—M. and R.

The organism was often found in gas gangrene in the war. See GAS GANGRENE.

Malta Fever. *Syn.* **Mediterranean Fever** or **UNDULANT FEVER.**

Mediterranean fever is treated chiefly with intestinal disinfectants—benzoaphthol, salol, urotropine, &c. The fever is almost completely wiped out from the Army and Navy by restrictions on goats' milk. (A very large proportion of the goats in Malta are constantly passing *M. Melitensis* in their milk). If the civil population were sufficiently enlightened to follow suit, there would probably be an end to the disease. Boiling the milk is all that is necessary, and the ortol and peroxide of hydrogen test is becoming popular as a means of proving that this is done where servants cannot be trusted.—H. Notes.

The fever is characterised by long irregular pyrexia, frequent relapses. There is profuse perspiration pains, and sometimes swellings in the joints, occasionally orchitis. Constipation is usually very marked. Incubation period 6 to 9 days. Temp. may be 106°, fatal 110° F.

In 1886 Bruce found *M. Melitensis* in the spleen of fatal cases of Malta fever, and by inoculating monkeys proved it to be the cause. Twenty years afterwards the fever was stopped, and no further diagnosis methods (by Widal's reaction) were required.

A large percentage of cow's milk samples taken at Greenwich gave + agglutination reaction with *M. melitensis*, presumably due to infection of the cattle with *B. Abortus*. About 5% of goats are still infected. To try to educate the people is a failure. Treatment should be a combination of Antitoxin serum and Autogenous Vaccine.—Surg. Rear Admiral Sir P. W. Bassett-Smith, *B.M.J.* ii. 22, 902.

M. Melitensis may be isolated from blood. Citrate 10 Cc. of blood, centrifugalise with Normal Saline twice and take up organisms and red cells with pipette; 1 Cc. added to tube of Agar at 40° C. and poured into Petri dish; several plates made and incubated at 37° C.; organisms picked out from 1st to 6th day.—*Jl. Trop. Med.*, April 1/24, 80.

Goats vaccinated intravenously with *B. Abortus* in massive doses protected from subsequent infection with a virulent *B. Melitensis* strain and fail to pass that organism in milk.—*Jl. Trop. Med.*, July 1/24, 195. (There is a degree of cross-agglutination between these organisms.)

Undulant Fever in the region of Tumbes, Peru, does not correspond with any of the well-known types and is not rare. The fly is thought to be the transmitting agent. The beginning of the disease is generally insidious,

resembling typhoid fever, but is sometimes sudden and accompanied by a cold fit. Perspiration is rare, while nausea and vomiting are very marked. Antiserums and autovaccines have proved efficacious in all cases.—Rebagliati, per JI. Trop. Med., Dec. 1/23, 358.

A case of undulant fever contracted in England.—L. ii./25, 1115.

B. Abortus infection in man. The illness in man may be very prolonged but prognosis is good. Vaccine treatment ineffective.—T. Thompson, L. ii./28, 1338.

See also H. Harrison and G. S. Wilson, L. ii./28, 1340. The more the disease has been looked for in the U.S.A. the more it has been found.—L. ii./28, 1349.

Malta Fever Vaccine.

Sometimes of service in cases with slight signs of intoxication where the pyrexia nevertheless tends to persist, also in cases of localised infection. 25—50 millions may be repeated in about 5 days, or sooner if the temperature fail to fall or tend to rise again. Prophylactic dose 1000 millions repeated or increased to 2000 millions. Interval 7 to 10 days. Total 5000 million advised.

Measles (See also Vol. I., pp. 996, 1076).

Bacteriology. Origin is ultramicroscopic. Prof. Caronia holds to a further cycle of development, in addition to the ultramicroscopic.—B.M.J. ii./23, 772.

SEROPROPHYLAXIS.—Methods of using serum to achieve passive immunity :

(1) Injection into healthy contacts ; immunity lasts a month.

(2) Injection during first 5 or 6 days of incubation period ; patient will not develop measles.

(3) Injection after 6th and before 9th day ; modifies attack.

(4) Injection at beginning of period of invasion (10th day) results only in local inhibition of rash.

Results decidedly favourable. Municipal collecting and distributing centres for serum established in Germany, France and America.

To produce active immunity, inject 10 Cc. convalescent serum and 24 hours later 1 Cc. of blood from an early case. If injection of blood is repeated, immunity may be permanent.—S. M. Copeman, B.M.J. i./28, 835.

In the common and fatal broncho-pneumonias and empyemas following measles in camps, *S. hæmolyticus* was found constantly. The importance of carriers of this organism in measles wards cannot be over-estimated. Cole found 11.4% of measles cases carried it on admission, 38.6% after 4 days, and 56.8% after 8 to 16 days. Cause of measles entirely unknown.—Stitt.

A review of recent work on measles.—J. E. McCartncy, L. i./27, 93-97.

A case recorded in which a child acquired immunity from measles as a result of injection of father's blood when suffering from melaena neonatorum 8 days after birth. It was discovered that the father had had a severe attack of measles in his youth. Suggested feasibility of preventing measles by injecting blood of adults who have contracted measles in childhood, instead of blood of convalescent children.—B.M.J.E. ii./24, 89.

The prophylactic injection of adult serum has been found to give approximately a similar protection against measles as 'M.R.S.' (Masern-rekonvaleszenten-serum).—L. ii./23, 615.

Milk Fever (In Cows).

It would appear that Calcium concentration in the blood is intimately connected with this disease of milk cows, goats, and sometimes ewes and sows. Dryerre and Greig put forward in 1925 the theory that as the parathyroid glands play an important part in regulating Calcium, and in the event of their functioning abnormally Calcium falls and tetany occurs. In Milk Fever there is a pronounced fall. Calcium injections and adequate Vitamin D in diet advised.—Veterinary Rec., Sept. 8/28, per C.B., ii./28, 462.

B. Mesentericus is the cause of ropiness in bread. It can be prevented by adding a little Acetic Acid to the dough (0.3 lb. per sack of flour). The *Watkins Test* is employed. To 7 sterilised test tubes add 1 to 7 Cc. of 20% suspension of the flour in distilled water which has been kept in a beaker in boiling water for ½ hour—to kill all organisms except the spores of the organism in question. Incubate at 28° C. for 24 to 48 hours. If the tubes indicate no ropiness at end of that time the flour is sound.—C.D. ii./17, 616.

Pellagra.

Pellagra is found in Europe, Africa, Asia, America, and even in Oceania, and probably affects more or less seriously over a million people. It is a disease of long duration, characterised by a peculiar rash, not unlike a severe sunburn which appears on the face, round the neck, and on the back of the hands and feet. This eruption recurs each year at determinate seasons (spring and autumn); it appears suddenly under the influence of exposure to sunlight, stands out some days, then fades off gradually, and is followed by long persistent desquamation. Together with the eruption other symptoms appear. They are irregular fever, frequent fits of giddiness with a peculiar sensation of falling backwards or forwards, great debility, confusion of mind, copious salivation, insomnia, pyrosis, and diarrhoea. These symptoms abate during the summer months and disappear almost entirely in winter, especially in early cases. They return with the rash each spring. After a period of progressive aggravation, which may last three, five, or thirty years, the patient becomes greatly emaciated, partly paralysed, and entirely demented. A number of these unfortunate beings commit suicide, as a rule by drowning; the majority end their days in the lunatic asylums of their respective countries. The disease affects the agricultural classes almost exclusively.

PELLAGRA FIELD COMMISSION.—Eating of Maize either sound or deteriorated can no longer be considered the cause of pellagra. A parasitic infection possibly conveyed by some insect. Pellagra occurs in districts where the sand-fly *Simulium* exists.—L. W. Sambon, L. ii./10,1709. B.M.J. ii./11,613.

Treatment by direct transfusion of blood. The recoveries (58%) following transfusion in the grave type of cases compares most favourably with the recoveries (10-20%) in the same type of case in which other therapeutic measures are employed. A few days after the transfusion gradual increase in body weight and improvement in mental condition was noticed. Recovery was established in a period varying from one to four months. No advantage has been noticed in the employment of a donor who has recovered from pellagra as compared with the donor who has never had pellagra.—B.M.J. i./11,1276; L. ii./11,526; see also Investigation of.—L. ii./10,1709; L. ii./11,556,1524. In Egyptian prisons they are now using maize bread.—L. ii./11,916.

Pellagra is not transmitted by contact or association of persons. Although in Europe only the rural inhabitants are affected, in America it occurs among urban residents and even the well-to-do are not immune. Of all drugs perhaps Arsenic has most value as a remedy—it is best given *per os* as Fowler's Solution increased to 20 or 30 minims three times a day. Intramuscular injections of Sodium Cacodylate, Sodium Arsanilate, and Arsacetin have given good results in early cases.—Charles R. Box, Pr. June, '13,940.

Pellagra in Great Britain.—An account of four cases with description of the histological changes in the nervous system, also a history of the disease. Sambon believes pellagra to be an insect borne infection probably conveyed by a species of *Simulium*, a biting insect which passes its larval and pupal stages in running water. The disease is common in Italy. It has been shown to be endemic to a limited extent at least in some of the eastern districts of Scotland north of the Forth.—C. R. Box and F. W. Mott, B.M.J. ./13,1. May become epidemic in asylums.—A. D. Bigland, L. ii./23,1295.

See also B.M.J. (Leader) ii./12,1155, *vide* also L. W. Sambon, B.M.J. ./13,119,297. also 570, 584. 1445 (Leader on Etiology). 1773.

Pellagra may be a **deficiency disease**. There are analogies between pellagra and beri-beri. The paper contains work dealing with guinea-pigs fed on good and bad maize plus cabbage.—Sandwith, L. ii./15,905.

Pellagra in Egypt. A syndrome occurring most often in the underfed.—A. D. Bigland, L. i./20,947, see also J. I. Enright, *ibid* 998, 1018. Also Helminthic infections as a factor.—H. M. Woodcock, *ibid*. 1193. H. F. Harris has issued a work on the subject which is well spoken of.—L. i./20,1272.

Deficiency of Protein.—W. H. Wilson, L. ii./20, 719, 765; see also *ibid*, 788

In Antigua Pellagra thought to be endemic. It is found among the blacks who live on cornmeal plus a generally inadequate and improper diet, not among the whites, who are really more susceptible to it, who eat cornmeal plus an adequate and varied diet. The facts indicate that while not incompatible with the theory that it is conveyed by *Stomoxys calcitrans*, they favour idea of **deficient food causes**.—W. M. Macdonald, L. i./15,127.

Pellagra and protein deficiency. Though it is a disease of the poor, starvation and pellagra are not convertible terms.—B.M.J. ii./21,1050.

Whilst diet deficient in protein and probably vitamin has been observed in most recorded cases, it is doubtful if this is the prime cause of the disease. The absence, especially of meat protein, from the patient's menu seems to be as frequently accounted for by its non-desirability as by its non-accessibility. Some outbreaks have been directly traced to faulty diet, and at least one—among the Armenian refugees at Port Said 1916-1917—has been stamped out by proper adjustment of the food deficiency.—See in particular numerous important papers abstracted.—T.A.B., Vol. 17, Feb. 14, '21, pp. 148-158.

DIET controls course and development of the disease. Suggested that the relationship is primarily due to a specific quality of the amino-acids make up of the protein supply.—J. Goldberger, *per. Jl. Trop. Med.* July 1/22 220.

Pellagra in children in England. Diagnosis, except in typical cases seen during Spring and Summer months when the rash is well marked, is not easy. Probably, a number of cases go undiagnosed. Nothing in the history to fit in with the various causation theories of pellagra. Both children in question had been fed on large quantities of 'Cornflour.' Good reproduction plates of rash. Pellagra ought to be borne in mind, especially in cases of diarrhoea with occasional dermatitis in children.—R. Hutchison and D. Paterson *B.M.J.* ii./23,646,670.

Treatment of 28 cases by addition of tomato juice, raw cabbage, lettuces and water in which vegetables had been cooked, to the daily diet; complete cure of all the patients.—*Jl. Trop. Med.*, Dec. 15/24,344.

Unbalanced diet not the only factor in etiology. The food factor, in lowering resistance, is an important predisposing cause. A full diet, rich in Vitamins B and C, with low Carbohydrate content, eliminating Cane Sugar, essential. Probably due to infection of some kind, when in condition of lowered resistance due to under-nourishment.—Seale Harris, *Int. Conf. Trop. Am.*, '24,719. C. C. Bass opposed to the theory of diet as factor. Experimental Pellagra in monkeys occurs in well-fed and well-nourished animals. He is convinced that it is infectious. Most cases get well spontaneously, and this has probably misled many, *ibid*, 720.

A review of researches on etiology. "Evidently the last word has not yet been spoken."—*Jl.A.M.A.* ii./25,212-214.

Pellagra is due to toxic absorption producing changes in nervous system followed by neuritis of certain peripheral nerves, which produces trophic changes in areas of skin supplied by affected nerves. Thyroid, 1 grain daily produced rapid improvement.—*Per Jl. Trop. Med.*, Feb. 1, '26,51.

From a pathologic point of view there is apparently an intimate association between alcoholism and pellagra.—*Jl.A.M.A.* i./28,371.

Five or six lemons a day will cure the average pellagra case in a very short time.—J. N. Roussel, *Jl.A.M.A.* i./28,371.

Earlier theories in earlier Edns., including the black-bird theory.—*L.* ii./12,251.

Pinta, a disease caused by a fungus, producing discolourations on uncovered parts of the skin.—*B.M.J.* ii./05,1270.

Pityriasis Versicolor, due to fungus growth under the skin, common in the tropics.—*B.M.J.* i./05,1271.

Bacillus Pestis (Bacillus of Bubonic Plague).

The Plague.

"The **symptoms** of plague in man develop within a few days of infection and consist of fever, headache, giddiness, weakness with staggering gait, great prostration, and delirium. In 75% of the cases the lymphatic glands in the groin, armpit, and other regions are inflamed, infiltrated and much enlarged constituting the 'buboes,' hence the name 'bubonic plague' frequently given to the disease. In the remaining cases the lungs may be primarily attacked the 'pneumonic' form, or a severe blood infection may develop, the 'septicemic' variety; in both of these buboes are absent, or are a late development if the patient lives. Occasionally an eruption of pustules or carbuncles appears on the skin, a phenomenon frequently mentioned by the older writers, and abscesses may form in the buboes. The bubonic form is hardly infectious or even contagious but the pneumonic variety is highly infectious, owing to the presence of large numbers of the infective agent the plague bacillus, in the expectoration from which it is readily disseminated

in the air. In some instances the patients do not appear particularly ill, and are able to go about, though such cases are liable to sudden death from heart failure."—T. R. Hewlett, Na., Dec. 23, 1911.

Out of 50,000 cases of plague in an epidemic in Manchuria only two or three undoubted bubonic cases were observed, all the rest were pneumonic. The duration of the disease was usually less than two days and no cases in which bacteriological diagnosis was complete were known to recover. Vaccination cannot be relied upon to give even reasonable means of protection against pneumonic infection. *An efficient mask affords the only reliable protection.*—Review of Tropical Diseases, Pr., Aug. '13, 218.

The Local Government Board issued a memorandum by G. F. Newsholme at the time of the outbreak in England. This draws attention to the infected eyes and thick drunken speech. For a criticism of this memorandum by G. F. Petrie, *v. postea*.

In addition there is the well-known tendency to "shouting" delirium and the impulse to patients to get out of bed and wander off, utterly heedless of their condition,—as seen in the natives of India.

For the **treatment** of plague are: 1. **Yersin's Curative Serum**, also used as a prophylactic. It is supplied by the Lister Institute in 20 Cc. bottles.

Dose.—At the earliest possible moment 50 Cc. intravenously and 50 to 100 Cc. intramuscularly or subcutaneously, *e.g.*, in the flank, repeated in 12 to 24 hours. 20 Cc. is given as a preventive. The Yersin Serum may be prepared by cultivation of a virulent growth of the bacillus obtained from several epidemics. An emulsion of the growth in physiological salt solution is injected intravenously into the horse in gradually increasing amount—the first few doses having the bacilli killed by heat. Bleeding takes place a fortnight after the last dose. The serum is finally tested for efficacy and not more than 0.35% cresol added.

After injection of Yersin's Anti-plague Serum the patient should be carefully warned that urticaria accompanied by rise in temperature, faintness and pain may follow. Rest and abstinence from alcohol are essential.—Luisi, T.D.B., Vol. 19, 1922/734.

The serum treatment of plague.—Jl. Trop. Med., April 1/24, 83.

Yersin prepared his original serum by injecting living bacilli, but this procedure has now been abandoned owing to its danger.—E. Lagrange, Jl. Trop. Med., Sept. 1, '26, 302.

2. **Haffkine's Plague Prophylactic (Plague Vaccine of the Lister Inst.)** This contains the dead bacilli preserved by 0.5% Phenol, as well as the products of their growth. The immunising substances are contained in the dead bacilli, *i.e.*, in the solid matter in the fluid and in the fluid itself. It is a killed culture of *Bacillus pestis*.

After injection there is local swelling and probably general malaise and heightened temperature. Immunity is conferred after 7 or 8 days by an injection, and it is advisable to inoculate persons exposed to infection every six months.

Dose.—For men 1 Cc., women $\frac{1}{2}$ Cc., for children over ten $\frac{1}{2}$ Cc., under that age 1/20 to 1/10 Cc. May be repeated in 10 to 14 days. **Site of Injection**—subcutaneously in any loose tissue free from veins, *e.g.*, the flank. *Shake the bottle.*

Since 1896 the Bombay Bacteriological Laboratory has issued 25 million doses of Haffkine's Vaccine. Statistics show a reduction in mortality by prophylactic injection of this vaccine of about 47%, in addition to which fewer persons contract plague among the inoculated than among the uninoculated. Several million lives have been saved by the use of this vaccine.—I.M.J., June, '25, 284.

Plague treated by (autogenous) Vaccine,—simple culture on Agar from patient,—dose being about 75 to 80 millions. Good result in non-septicaemic cases. 79% recovered.—R. Row, B.M.J. ii./13, 1021.

Statistics showing value of prophylactic Anti-plague vaccination. No cases that were vaccinated died.—M. Kiamil, T.D.B., Vol. 19, 1922, 728. See also B.M.J. ii./10, 1658.

Yersin's bacilli obtained from glands of healthy inhabitants of Dakar who had been in contact with plague.—M. Leger and A. Baury, *per* Jl. Trop. Med., June 15/23, 226.

Bacteriophage therapy should constitute the specific treatment for plague

from 1 to 2 Cc. of a very virulent bacteriophage culture being injected as soon as possible. Four cases of bubonic plague recovered rapidly following injection into the buboes.—F. d'Hercle, *Presse Med.*, Oct. 21, '25, per *Jl.A.M.A.* ii./25,1653,1762.

In 1908-9, 1,491 cases of bubonic plague were treated in Guayaquil, Ecuador. Patients not receiving anti-plague serum gave death-rate of 60%, as against 33% of those who received it. Where treatment could be given within 24 to 36 hours of onset, mortality might be reduced to 18 or 20%. Fresh serum essential.—B. J. Lloyd, *Jl.A.M.A.* ii./25,731.

Bacteriology.

Morphology.—Short fat bacillus. On staining with weak aniline dye shows marked polar staining. Spores have not been demonstrated. Non-motile. Does not retain the stain when treated by Gram's method; grows well on usual media both at room and body temperature. Does not liquefy gelatin. Occurs in chains when grown in fluid media. Forms typical stalactite growths in bouillon and in presence of butter fat, but must be kept undisturbed (Haffkine). Man is inoculated through the broken skin.

The bacillus produces alkali in its growth equivalent to 1.5 to 2.5% normal Sodium Hydroxide Solution, in 6 to 8 weeks. This effects arrest of growth, but not death of the bacillus.

In smears made at an early stage of the disease from the buboes, expectoration or blood respectively in the three varieties of plague, the bacillus is present in enormous numbers, and the films show "polar staining," the centre being hardly stained at all; this is characteristic. In older lesions peculiar, large rounded or ovoid "involution" forms of the bacillus are met with. The organism is readily destroyed by heat (60° to 65° C. for ten to fifteen minutes), and by disinfectants. The plague bacillus is pathogenic for a number of animals, in addition to man—the rat, mouse, guinea-pig, rabbit, hare, ferret, cat, monkey, etc. In the United States the ground squirrels are attacked.—R. T. Hewlett.

Concerning the discovery of the plague bacillus.—E. Lagrange, *Jl. Trop. Med.*, Sept. 1, '26,299.

Epidemiology.

The flea, usually *Xenopsylla cheopis*, is the transmitter from rat to rat and from rat to man.—L. ii./26,632. Clinical experience shows that plague has no preferential temperature, though the Third Report of the Plague Commission sought to establish a "climatic plague temperature" of 85° to 50° F. Calcutta is remarkably free from human fleas; dog fleas are prevalent on the other hand, and rat fleas are seldom or never found. Rat fleas do not bite men, on the contrary they have a strong distaste for the skin of man. Evidence of equally conclusive nature in the opposite direction by a Member of the Commission. There is always an association between rats and plague in India. *Further data in 18th Edn., Vol. II. p. 540.*

The character of the disease seems to change from bubonic in summer to pulmonary plague in the cold season.—L. ii./11,1311.

Notes on the L.G.B. Memorandum on Plague.

The "ambulant" type may spread the infection, but it is doubtful if this occurs by direct personal contagion, and it is equally doubtful whether effective carriers of the disease in the sense of typhoid carriers exist. The evidence for the existence of such carriers is not satisfactory, and although the possibility of the occurrence of "pneumonic" carriers must be considered, the rarity of this type, at least in India, and its extreme fatality, considerably limit its importance from this point of view.

There is little or no liability to infection from contaminated food. The memorandum deals fully with rat destruction. Kitasato reported that in five years 4,800,000 rats were killed in Tokio alone at a considerable financial outlay, but that at the end of this time no appreciable decrease in the rat population could be detected owing to the natural increase, but rats in this country should be exterminated as possible source of danger.—G. F. Petrie, *Na.*, Nov. 19, '10,81.

The Plague in China and the far East in the winter of 1910 and early spring of 1911, was of the **Pneumonic Type**—the more severe form—a very large proportion of the natives and Europeans attacked died. Up to April, 1911, the outbreak claimed 46,000 victims. The first outbreak in the winter of 1910 was among hunters of the rodent *Arctomys bobac*, known in English

as the marmot, in Russia as the tarabagan, and in Chinese as the hanta,—an animal susceptible to epizootic plague infection. It was spread by these men returning home. The extreme cold induced an indoor existence, so parties of coolies travelling through the country slept under conditions of constant intimate contact—there is little evidence of infection having been contracted in the open air. Those towns that had adopted preventive measures before they became badly infected practically escaped. Isolation of patients and their contacts, and disinfection, when efficiently carried out, have invariably been followed by diminution of the death-rate. Amongst the rats examined no instance of plague infection was found.—International Plague Conference, L. i./11,1117 1118,1152,1162. See also L. i./12,688.

The proportion of pneumonic cases in this epidemic caused alarm; *As the only true infectious cases are the pneumonic.* Though latest experimental evidence indicates that bubonic plague can only be caused by infected fleas yet the writer has seen the transmission from the pneumonic to the bubonic without rats or fleas. The happiest thing to occur regarding the outbreak would have been for this pneumonic outbreak to become bubonic,—combined with the enforcing of sanitation in the infected area so as to limit the spread of the epidemic.—Pr., May, '11, p. 623.

Flea infected clothes in India are spread on sand in the direct sunlight, in 5 minutes all are killed.—B.M.J. i./11,1293: P.J. i./11,740.

History and Etiology of the plague.—Lt.-Col. W. Glen Liston, B.M.J. i./24, 900,950.

PLAGUE AND ENGLISH LIFE.

The effect of plague in the past upon English national life has been very deep. Every English hedgerow is a reminder of plague. The hedgerows mark the change in land tenure which followed the Black Death. The pestilence produced a scarcity of labour which gave the final blow to villeinage and serfdom, and when farming in common ceased it became necessary to define the fields. From that period dates the emancipation of the English labouring classes. Plague helped to kill the textile industries of the Eastern Counties and laid the foundations of the modern prosperity of Lancashire and Yorkshire. It was largely responsible for the decline of the power and wealth of the monasteries, and thus brought nearer the Reformation. It facilitated the growth of English literature. Up to the time of the Black Death, French was the principal language of the schools and of the wealthy. So many teachers died in the epidemic that a new race of educationists arose who insisted on giving instruction in the English tongue, and the way was thereby paved for "Piers the Ploughman" and Chaucer. Europeans are no more exempt from plague than Asiatics. Their only protection is that their mode of life does not bring them into close contact with rats, or with the rat fleas.—From a news article on the scattered outbreaks in England in 1911.

The Tarbagan (Mongolian Marmot) and plague. Exhaustive investigation into its possible cause of spread of plague. Not nearly so important as the rat—in this respect almost negligible.—L. ii./13,529.

Varieties of rat fleas spreading plague.—L. ii./21,1287.

Transmission of plague by fleas. *Xenopsylla astia* probably the sole rat flea relatively immune to plague.—L. Fabian Hirst, per Jl. Trop. Med., April/23,114.

Plague sputum is extremely resistant to Carbolic, Lysol, Sublimite, Potassium Permanganate, Hydrogen Peroxide, Alcohol, Methylated Spirit, etc. Pneumonic Plague is a direct infection from man to man. Infection is carried in a droplet form—when moist sputum is thrown out during coughing, talking, etc. Crude Sulphur burnt after the walls have been sprayed with water is best for fumigating houses. Floor containing sputum covered with slaked lime. Clothes and overalls fumigated with Formalin gas made by warming 100 Gm. Permanganate, 100 Gm. hot water and 200 Gm. Formalin in a pot.—L. Tuck, L. ii./21,853.

PLAGUE IN MANCHURIA. *B. pestis* present in plague sputum killed within 4 hours by direct sunlight at a winter temperature (-3°C). Carbolic Acid solution 1 in 10 requires 5 minutes to prevent growth of *B. pestis* in sputum.—L. L. Teh, Jl. Trop. Med., Aug. 1/23,256. #

PLAGUE IN ASTRAKAN. Camels an important source of infection in man owing to their eating hay and green fodder infected by mice and ground squirrels.—S. M. Nikanorov, per Jl. Trop. Med., April 16/23,128.

Bubonic plague is a disease of rats, and the human case is, for all practical purposes, not infectious. Abundant evidence that bubonic and pneumonic plague are entirely separate and distinct epidemic diseases. It is doubtful whether plague bacillus alone can cause pneumonic plague epidemics, which are probably caused by the bacillus in symbiosis with another organism, probably non-pathogenic for rodents. Control of grain trade and the proper storage of grain in 'rat-free' stores almost synonymous with efficient plague preventive measures. Disinfection of houses, etc., the most common of all anti-plague measures, excites great antagonism and is of doubtful value. Attention paid to the usual channels of infection could secure almost absolute immunity from plague, without restriction to the free flow of commerce.—N. White, Report to Health Committee of the League of Nations, per Trans. Roy. Soc. Trop. Med., Vol. 17, No. 8, Feb., '24, p. 525.

PLAGUE IN BAGHDAD. It is endemic in that district and is determined by climatic conditions. The protection by anti-plague vaccine is definite and almost complete—some protection may last even longer than 1 year. The best method of treatment is by the anti-plague Serum (Pasteur)—large doses intravenously in toxic cases as soon as possible. Doses of less than 40 Cc. are useless and in very toxic cases 100 Cc. are required.—T. B. Heggs, JI. Trop. Med., Nov. 1/23, 328.

Pneumonic plague in Iraq.—T. B. Heggs, Trans. Roy. Soc. Med., Vol. 18, No. 1, May, '24, 45.

PLAGUE IN EGYPT—a review of its past and recent history.—B.M.J. i./24, 582; *ibid.* 900.

PLAGUE IN INDIA.—During the years 1898-1918 plague carried off a total of 10,254,221 people—an annual average of over half a million.—I.M.G., June, '25, 277.

Evidence is conclusive to incriminate the Asiatic tarabagan, or bobac, as carrier of pneumonic plague.—L. ii./24, 330.

Pneumonia.

The source of the Pneumococcus and Modes of Infection, Pneumococcus Vaccine, Prophylactic Inoculation, Types of the Pneumococcus and Serum are dealt with, Vol. I., p. 924, et seq. See further Influenza, Vol. I., p. 921, and this Vol., also Therap. Ind. Vol. I.

Fraenkel's Pneumococcus.—1. Prepare films from 'rusty' portion of sputum. 2. Stain by Gram's method and counterstain with eosin half to one minute. Stain other films by carbol-fuchsin. Overstain (five minutes). Slightly decolourise with weak acetic acid. (For capsule.)

To obtain a pure culture, the blood of a mouse dead from inoculation of sputum is sown on blood agar or Nasgar medium. Will not grow below 37° C.

Recognition.—Diplococcus (ends are often pointed—*Diplo lanceolatus*) sometimes occurs in short chains of four to ten cocci. Has a capsule, but this is absent in cultures. Gram +.

This organism is the cause of more than 80 % of lobar pneumonia.

The best medium for differentiating is the serum of a young rabbit, in which it grows as a diplococcus, while streptococci show chains. On plain agar it grows as a very small dew-drop-like colony; slightly greyish by reflected light. It produces considerable acid and coagulates litmus milk. Acid is produced in Inulin media which streptococci fail to do. The most important differentiating point is its solubility in bile.—Stitt.

Pneumococcal peritonitis usually sets in suddenly; acute pain is common, vomiting usually present, stools loose and temperature high. The urine is diminished and contains excess of carbonates, phosphates and traces of albumen.—B.M.J.E. i./27, 109.

CONJUNCTIVITIS, BACTERIOLOGY OF.—In a school outbreak an organism morphologically identical with the pneumococcus but differing in fermentative activity and its non-pathogenicity to animals, usually highly susceptible—L. ii./11, 1418.

In cataract cases (at Prague) examination for pneumo and streptococci by growth in **Elschnigs' Culture Medium**, *vide* Culture media, is made and if found operation postponed with hourly applications of 1 in 5,000 Mercury Oxycyanide Solution until the organisms have disappeared. Simultaneously an Agar culture is made for diagnosing variety of Staphylococci if present.—E. W. Thomson, Glas. Med. JI., Feb., 1913.

Growth of the pneumococcus: Sir A.E. Wright's Serum Glucose Broth. 1% Peptone, 1% Lemco, 2½ to 5% of human serum and an amount of alkali fixed by neutralising to Phenolphthalein and then adding 6 Cc. of normal acid to each litre of medium. 1% Glucose was found a valuable addition—the broth so made gave copious growth of pneumococcus.—L. i./14,1.

Friedlander's Pneumobacillus. *Syn. B. Mucosus Capsulatus.*—Present in only small proportion of cases of pneumonia. Common in influenza. Gram —, but stains well by carbol fuchsin.

Recognition.—A bacillus varying considerably in length; usually short with rounded ends. Non-motile, usually $1 \times 2.5\mu$. Has a capsule. Is easily cultivated on all ordinary media.

Produces gas in Glucose media, but not in Lactose bouillon; differentiation from *B. coli*. In a Gelatin stab it presents a 'nail' appearance, the growth at the surface being heaped up like a round-headed nail and the line of puncture resembling the shaft. It is best examined by dark ground or parabolic illumination. Stain by Gram's method but do not wash with alcohol and omit any counter-stain. Hot Acid-Fuchsin gives good results.

Serological characters of types of pneumococci.—R. H. Armstrong, B.M.J. i./21,259.

Pneumococcal infections—the bacteriological aspect.—J. H. Dible, L. i./24,8.

Sterile broth extracts of unwashed pneumococci, free from living or intact cells, actively reduce Methylene Blue.—Jl. Trop. Med., Dec. 15/24,346.

The soluble specific substance of pneumococcus. Weight of evidence is in favour of view that specific substances of pneumococcus Types II and III are actually polysaccharide derivatives.—Jl. Trop. Med., Dec. 15/24,346.

Pneumonia incidence and climate in India.—Sir Leonard Rogers, L. i./25,1173.

The organism is the probable causal agent of pseudo-membranous bronchitis, chronic bronchitis and pseudo-pneumonia.—B.M.J.E. ii./27,79.

Polyomyelitis. (Inflammation of the gray matter of the spinal cord.) The virus of polyomyelitis stands midway between the finest and coarsest examples of 'filterable viruses.' It is highly resistant to drying, light and chemical action. In dust, especially with protein matter, it survives weeks and months—in diffusive daylight indefinitely and it resists the action of Glycerin and Carbolic Acid in 0.5% solution for months.—S. Flexner, L. ii./12,1451,1790.

Three clinical stages of evolution of poliomyelitis—general infection, during which the virus enters the liver, spleen, and lymphatics, invasion of the sub-arachnoid space, and thirdly invasion of the central nervous system itself, this last phase producing paralysis. During the second stage the cerebro-spinal fluid gives a meningeal reaction and its cell count ranges from 30–2,000 cells per cmm. The blood reveals a leucocytosis in most cases, the total white cell count rising as high as 25,000, with a relative predominance of polymorphonuclear cells.—F. M. R. Walshe, L. i./27,326.

A good series of clinical pictures of poliomyelitis.—J. Collier, L. i./27,321.

In 75 cases, 43 of which were undoubtedly poliomyelitis, 35 obtained milk from the same source, the remaining 8 taking their supply from a dealer who, owing to temporary shortage had purchased daily a supply from the other dealer. Although the evidence of milk transmission is not conclusive it must not be too lightly dismissed.—L. ii./27,1190.

Convalescent Serum.

Intramuscularly of distinct value, its effectiveness depending on early diagnosis and injection of sufficiently large, and if necessary, repeated doses. Owing to its safety and simplicity it can be used in doubtful cases.—B.M.J. ii./28,501.

ACUTE POLIOMYELITIS.

Infection may be conveyed by (1) persons suffering from an acute attack, (2) persons having a mild or atypical form, (3) healthy contacts who have not developed an attack, and (4) chronic carriers who have apparently recovered from a previous attack.—A. S. MacNalty, L. i./25,478.

Epidemiology.—In 1918, 228 cases were notified in England and Wales, the larger proportion being between 1–5 years old. Usually one attack produces permanent immunity. The incubation period appears to be from 2–10 days.—*ibid*, 536.

Polio-encephalitis in which the lesion chiefly or solely involves the upper motor neuron, giving rise to spastic paralysis, is a rare disease, but has also been described.—*ibid*, 537.

Acute poliomyelitis, with references to the occurrences at the Royal Military Academy and at Uppingham School.—Jl.R.A.M.C., Mar., '27, 215, *cf.* Vol. I. p. 1085.

See also *Encephalitis and Encephalitis lethargica*, p. 543. }

Bacillus proteus vulgaris occurs frequently (50% of examinations) in chronic aural discharges and is frequently present in the stools, etc. It stains easily with the usual stains and is Gram negative.

Rabies. **HYDROPHOBIA** is an acute infectious disease communicated to man by bites of animals suffering from rabies. Cauterize the bite wound with strong Nitric Acid as quickly as possible, even if the Pasteur Vaccine can be given.

Antirabic Vaccine. A dead Carbolized Rabies Virus made by Sir David Semple's method can be sent to any locality, where treatment can be carried out, without losing its properties.

A Central Institute could supply the whole of India with Vaccine, patients would hence be saved long journeys to Pasteur Institutes where the preparation of living vaccine is carried on. Most important of all, the treatment would be early,—this is the essence of success, and the treatment is free from all risks.—*Vide* Sir D. Semple, *Sci. Memoirs by Officers of the Med. and San. Dept. of the Indian Govt.*, 1911, also L. ii./11, 173.

A rapid method of anti-rabic treatment by etherized vaccine.—B.M.J.E. ii./25, 14.

Cultivation.—H. Noguchi, by the method used for isolating the spirilla of recurring fever, isolated two forms of micro-organism from cultures prepared from the brain or spinal marrow of animals infected with hydrophobia. One is a minute corpuscle almost ultramicroscopic, the other, which is constantly reproduced in successive cultures, a larger nucleated corpuscle which more resembles protozoa than bacteria. These nucleated corpuscles multiply rapidly both by budding and fissure. They vary from 1 to 12 microns and by the ultramicroscope show a central nucleus surrounded by a very distinct refringent membrane. Inoculation with cultures, in which either the granular or the pleomorphic organisms predominated, caused the death of the animal with all the typical symptoms of rabies.—*Presse Medicale*, 1913, (73)729, per P.J. i./14, 219.

Rabies and Antirabic Treatment.—Sir D. Semple, B.M.J. ii./19, 333, 371.

Hydrophobia in Egypt—with special reference to diagnosis.—R. V. Dolbey and A. E. Katib, L. i./24, 538.

Good results obtained by *intravenous* injection of antirabic vaccine. Rate of injection should not exceed 0.5 Cc. a minute, the dose being 2 Cc.; there are no local or general symptoms following use. 96 cases treated, with 5 to 7 doses intravenously, with one death. Treatment may be regarded as safe.—B.M.J.E. i./25, 2.

Two Japanese workers—Umeno and Doi—introduced a method of immunising dogs by a single injection. The vaccine is prepared from the brain and cord of a rabbit dying from a laboratory strain of rabies which kills the animal in 7 days, *i.e.*, a “fixed virus.” To the ground-up nerve tissue is added 4 times its volume of a phenolised glycerin-saline solution, and the mixture kept for a month in an ice-chest to reduce its virulence; it keeps for two or three months at room temperature. In Japan over 30,000 cases have been vaccinated with only one failure, and in the areas where it has been used rabies has been reduced already by 75%. Equally successful results obtained with the vaccine in U.S.A.—Leader, B.M.J. i./24, 1060.

Relapsing Fever, Syn. Recurrent Fever, is associated with the presence of *Spirochata Recurrentis*, *Syn. Borrelia recurrentis*, *Spirillum Obermeieri* in the blood. In cases of relapsing fever terminating fatally the blood is frequently found to be teeming with the organisms. The corpuscles with the $\frac{1}{12}$ inch oil immersion lens frequently appear to have slender spiral filaments attached to them, causing a rippling movement of the blood which persists for several hours when examined in the fresh condition.

African Relapsing fever. Transmission by Ticks.—B.M.J. i./13, 65.

Noguchi cultivated four species of pathogenic spirochetes occurring in the blood (as distinct from those which invade tissues—*Sp. Pallidum q.v.*, and that of yaws). The pathogenic blood Spirochetes cultivated include *Sp. Obermeieri* which is the cause of relapsing fever in Europe and the spirochaete of the fowl. He also has grown (nonpathogenic) Saprophytic Spirochetes, e.g., *Treponema macrodentium*, *T. microdentium*, *T. mucosum*, *T. refringens* and *T. calligyrum*—a new species standing morphologically between *T. pallidum* and *T. refringens*.—B.M.J. ii./13,1100.

S. Hata cultivated Spirochetes of Recurrent Fever in a medium containing Horse Serum and buff coagulum. The virulence of cultivated spirochaetae is relatively weak. Sir Wm. Leishman showed evidence of granule shedding in spirochaetosis and the development of the spirochaeta from the granule.—Int. Cong. of Medicine, 1913, L. ii./13,569.

Wenyon mentions 12 species of relapsing fever spirochetes.

Infection in lice by the spirillum of recurrent fever is hereditary, contrary to previous views. The spirilla occur in the lacunary cavity of the insect not in the mouth organs or digestive apparatus. Inoculation does not take place from bites but through wounds in the animals caused by scratching. The animals become infected by the nails with fluid from crushed lice.—Ann. Inst. Pasteur per P.J. ii./13,729. A human being who had allowed himself to be bitten 30,000 to 40,000 times with infected lice never became infected, as care had been taken not to damage the insects. Only occasionally does infection pass through the eggs of lice to the succeeding generation.—Wenyon, 1253.

Kligler and Robertson (1922) found the following *medium successful* for the growth of *T. recurrentis* (relapsing fever spirochete): horse or rabbit serum diluted with 1 or 2 parts of saline solution, or undiluted ascitic fluid: to each 10 Cc. of this fluid is added 1 Cc. 10% Peptone Broth; reaction adjusted to pH=7.2: place 3 to 4 Cc. of the mixture in each test-tube. Inoculate with a drop of blood or 0.1 Cc. fluid from a previous culture, and cover surface with a layer of oil. Aristowsky and Holtzer (1924) used a medium prepared by adding 8 Cc. saline solution to 4 Cc. young horse's serum in a test-tube and introducing a piece of blood-clot or white of hard-boiled egg: inoculate and incubate at 35° C.: subculture every 48–72 hours.—Wenyon, 1257.

Indian Ink method of staining is best.—cf. Syphilis Chapter.

Relapsing Fever in Palestine.—W. K. Calwell, L. ii./20,785.

Wassermann reaction in relapsing fever. 11 out of 18 cases gave positive reaction. Transient positive reaction may be expected during acute stages of relapsing fever.—Brit. Jl. Experim. Path., per Jl. Trop. Med., Aug. 15/22, 264.

Relapsing Fever in the Treatment of G. P. I.

Blood taken from the tail or heart's-blood of an infected mouse, mixed with Saline and injected hypodermically or intravenously. Incubation period: hypodermically, 5 to 7 days; intravenously, 2 to 3 days. Three to five chills usually occur with rapid rises of temperature. Intervals between febrile symptoms usually 6 to 8 days. Disease allowed to end naturally in 6 to 8 weeks, and cannot be checked by Arsphenamine. Danger of contagion slight. Severe heart complications and severe general debility the only contraindications. Early treatment best, but even advanced cases favourably influenced. Results from malaria and relapsing fever treatments about evenly balanced.—Jl. Trop. Med., Jan. 16/28, 23.

See also Tick Fever, *postea*.

Ringworm Fungi. Rapid Clinical Method of Search:—

- (1) Soak the hairs in Potash Solution for 10 minutes.
- (2) Wash in water to free from Alkali.
- (3) Mount in Glycerin or Glycerin Jelly.

For permanent stained sections.—

- (1) Soak the hairs in Potash Solution for 10 minutes.
- (2) Stain with Aniline Gentian Violet (*q.v.*) for 1 hour.
- (3) Absorb excess of stain.
- (4) Treat with Gram's Iodine Solution 2 minutes, wash in water. Decolourise with acidified Aniline Oil (Aniline Oil 10, Nitric Acid 1) for 15 to 20 minutes. Treat with Aniline Oil 1 minute, clarify in Xylol, and mount in Balsam.

The organism of *Favus* is *Achorion Schonleinii*; those of *Tinea tonsurans* RINGWORM OF THE SCALP and *T. circinata* (RINGWORM OF THE BODY)

i.e., non-hairy skin, are *Microsporon Audouini*, *Tricophyton Megalosporonectothrix*, and *endothrix* (according as the fungus lies outside or inside the hair); that of *Tinea versicolor* (Pityriasis) is *Microsporon Furfur*.

Ringworm of the Scalp is rare in the adult.

Tinea Barbe or *Hyphogenic Sycosis* (Ringworm of the beard) is a common affection of the beard. The common grey coccus inhabiting the upper layers of the epidermis may cause an infection and cause pustulation, but the fungus can be distinguished from this coccigenic variety. Syphilis may also sometimes simulate ringworm of the beard. *Eczema Marginatum* is a name for ringworm attacking the groins and axillæ. *Onychomycosis* or ringworm attacking the nails only—not common, but very troublesome.

Cultivation of Ringworm Fungi is possible on all ordinary media, but the addition of Glucose or Maltose is most favourable.

Contagiousness of Favus in man.—R. Sabouraud, L. ii./19,581.

The importance of symbiosis in production of certain biochemical phenomena and causation of certain diseases and symptoms of disease. Certain diseases are caused by true symbiosis, e.g., Trichomycosis rubra, trichomycosis nigra and stomatitis cryptococcus bacillaris. The mousy smell of favus is not caused directly by the fungus but by associated organisms; the honey-yellow crusts of yaws caused by pyogenic cocci associated with the specific germ. The abdominal distension in certain cases of typhoid caused or increased by association of *B. Morgani* to typhoid bacillus.—A. Castellani, Jl. Trop. Med., Aug. 2, '26, 217–226.

See also *Dhobie's Itch*, p. 534.

Scarlatina or Scarlet Fever.

In most cases, with or without albuminuria, *Streptococci* are voided by the urine in large quantities in this fever.

Streptococcus Conglomeratus Vaccine is prepared. See Vol. I. p. 929.

Various Drugs, taken internally or used locally, may occasionally, especially where idiosyncrasy exists, produce scarlatina-form rashes, e.g., Venice Turpentine applied.

Schultz-Charlton Blanching Test.

Ordinarily, 0.2 Cc. of a 1 in 10 dilution of Scarlet Fever Antitoxin made in the horse is injected intradermally into the chest, abdomen or forearm, where a uniform scarlet fever rash not more than 70 hours old is available. A blanching 10–40 mm. in diameter appears 4–10 hours later and persists from 12 to 72 hours in most patients suffering from scarlet fever. Other workers inject 0.5 or 1 Cc. either diluted or undiluted. The dilution should not be used more than 6 months after preparation. If the patient's serum taken 10 days after an attack fails to produce the Schultz-Charlton blanching in scarlet fever patients the evidence that the disease was not scarlet fever becomes practically conclusive.

The reaction, as described by Schultz and Charlton (1918), is very striking.—W. Mair, L. ii./23,1390.

BACTERIOLOGY OF SCARLET FEVER.

Mervyn Gordon pointed to 3 distinct types of hæmolytic streptococci.—B.M.J. i./21,632; ii./23,772. Gordon's Type III. (*S. scarlatinae*) is found chiefly in tonsils and fauces of scarlet fever patients and is quite distinct from the more common hæmolytic *S. pyogenes*. The work has been carried further by Coronia and Surdoin, who have conferred immunity on children, as also by Takahashi of Tokyo, and A. F. Dick and G. Dick.—B.M.J. ii./23, 772. See also our Vol. I., p. 929.

Dick Test Technique.—

This resembles the Schick Test and consists in injecting intradermally into the left forearm 0.2 Cc. of a dilution of the filtrate obtained from a broth culture of *Streptococcus scarlatinae*. A control of boiled fluid is injected into the right forearm in the same manner. A definite flush about 10 mm. or larger in diameter, coming on in 4–12 hours, and lasting for 24–72 hours is regarded as a positive reaction.

A private body called the Scarlet Fever Committee is to take out patents for the purpose of isolating the hæmolytic streptococci specific for scarlet fever, and for growing them, obtaining therefrom the toxin, and the antitoxin specific for scarlet fever, for the process of standardising and identifying the antitoxin, for the method of using the human skin for tests, and for other

connected purposes. Such patenting of biological processes strongly deprecated.—B.M.J. i./27,479.

Patients giving skin tests showing susceptibility to scarlet fever injected with quantities of the toxic filtrate of the hæmolytic streptococcus might develop rash and other scarlatinal symptoms within a few hours of injection. Within 48 hours symptoms disappeared and skin test found negative. Authors consider these results due to soluble toxic substance rather than to filtrable virus and indicate production of a degree of active immunity.—G. and G. Dick, J.A.M.A., Jan. 26/24,301,264; B.M.J. i./24,339,482.

The hæmolytic streptococcus of scarlet fever resembles others in morphology. Their specific toxin can be recognised. Method of doing it is detailed (Dick's work).—B.M.J. i./25,792.

References to the Dick Test.

The method of immunisation recommended by the Scarlet Fever Committee (U.S.A.) requires 5 doses of 500, 1,500, 5,000, 15,000 and 20,000 skin test doses of toxin as minimum, respectively, with interval of one week between doses—but three injections of 500, 5,000 and 30,000 respectively, with two weeks intervals, found as effective.—C. C. Young and P. F. Orr, J.A.M.A. i./26,1342.

Description of the Test.—A. B. Porteous, Pr., Jan., '26,83. A scarlet fever toxin for the Test.—Per J.A.M.A. ii./25,1014. Etiology, prevention by immunisation, and antitoxin treatment.—W. H. Park, J.A.M.A. ii./25, 1180-86. A clinical study of the Test. 'Scarlets' in the first five days of illness yielded a + % of 95.15, whereas from the 31st to the 35th day 4.76 were found +.—A. Joe, L. ii./25,1321; see also F. A. E. Silcock, L. ii./25,1327 and 1334 (Leader). Dick prophylaxis of scarlet fever largely used in U.S.A. and Canada.—B.M.J. ii./26,845. The Test is of no value for diagnosis of scarlet fever but shows whether or not child is immune to that disease.—Per Pr., July, '26,65. Encouraging results.—C. B. Ker, J. E. McCartney and J. McGarrity, L. i./25, 230. See also *ibid*, 710,712. Therapeutic results of concentrated Scarlet Fever Antitoxin.—G. F. Dick and G. H. Dick, J.A.M.A. ii./25,1693.

Scarlet fever antitoxin in proper amount a specific and prompt cure for uncomplicated scarlet fever. To be therapeutically efficient in reasonable dosage, an antiscarlatinal serum should contain at least 12,500 minimal blanching doses of antitoxin per Cc., or be able to neutralise at least 10,000 skin test doses of toxin per Cc. The amount of antitoxin required to cure scarlet fever promptly and with certainty, by intramuscular injection, varies from 3,000-12,000 units (30-120 Cc. of a serum which neutralises 10,000 skin test doses of toxin per Cc.), depending on size of patient and severity of disease. To obtain best results, the full amount required should be estimated and given at once, as soon as diagnosis is made.—F. G. Blake and J. D. Trask, Boston Med. & Surg. J., Oct. 8, '25, per J.A.M.A. ii./25,1584.

Hæmolytic streptococci and scarlet fever. Can be differentiated from those of erysipelas, septicæmia, puerperal fever, etc., by agglutination methods.—R. A. O'Brien, B.M.J. ii./26,513.

Production of antiscarlatinal serum.—Nat. Med. J. China, per J.A.M.A. i./25,1432.

Efforts to show that in serological characters scarlatinal streptococci are identical among themselves and differ from all other streptococci have so far failed—the streptococcal species is too heterogeneous and perhaps too unstable. Further work on streptococcal toxins is in progress.—A. Eastwood Min. Health Rept (No. 35), C.D. ii./27,385.

Serpent Venom. Anti-venene.

In the preparation of this serum the venom is removed either from the living snake or after killing it. This venom is mostly desiccated over sulphuric acid *in vacuo* and a weighed quantity of this is dissolved in sterile water and injected into the horse. The increase in dose proceeds very gradually; the final dose appears to be about 0.6 Gm. of venom, equivalent to the entire yield of 20 average sized snakes. The serum is removed in the customary manner and standardised.

Calmette showed that the venom of all snakes is of a similar nature, and obtained his remedy by the inoculation of horses with the poison of the cobra *capello*: his serum possesses a strength of 1 in 20,000: that is to say $\frac{1}{20,000}$ Cc. subcutaneously injected into a hare of two kilos in weight suffices to protect it from snake poison which kills a similar hare in eight hours.

It is said that anti-venomous sera are specific even between the venoms of a species of the same genus.

Calmette described the hæmolysins of snake poison; in addition to these bodies snake poison contains neurotoxins, which act on the nervous system and cytolsins dissolving other tissue elements.—Bull. de l'Inst. Pasteur 'T.

Dose.—Anti-venene is supplied in tubes of 10 Cc. This amount or as much as 40 Cc. should be injected. The serum should be as fresh as possible. (As much as 400 Cc intravenously and 10 or 20 times that amount, if subcutaneously, has been advised for cobra poisoning). The injection made within an hour in man; death seldom occurs from serpent poison under 3 hours.

A ligature must be bound above the bite if possible. The wound should be opened up and washed with Chromic Acid or Gold Chloride 1% solution.

Difficulty of obtaining sufficient venom—200 rattlers required to secure 60 Cc. venom. A preparation from blood rendered immune to mixed poison of S. American vipers and called "Vital Brazil polyvalent Anti-Bothrops" proved as efficient as Calmette's serum.—L. i./27,244.

In England adder bites were successfully treated with Antivenene in the summer of 1929.—W.H.M.

Liq. Strychninæ, 20 m. hypodermically, of value in snake bite.—J.M. C. Gray, B.M.J. ii./29,600.

Sleeping Sickness. see **Trypanosomiasis.**

Sporotrichosis (due to *Sporotrichon beurmanni*).—Has been treated by liberal doses of Potassium Iodide, e.g., 80 grains per diem. Locally Iodine in the form of Gram's Solution is useful. The Iodine appears to act indirectly by stimulating absorption. Cultural characteristics and peculiar properties of the fungus suggest that it may be overlooked. The fungus produces glistening subcutaneous tumours which may ulcerate. In all granulomata which cannot be clearly attributed to the ordinary causes of such lesions the possibility of Sporotrichosis should be kept in view.

Sporotrichosis of the eyes, a number of cases. Sporothrix isolated from the pus from broken down nodules. Large doses of Potassium Iodide followed by rapid improvement both of the iritis and general condition.—Oph., 1911.

Beurmann states that there are several Sporotrichoses according to nature of the numerous parasites cited. That due to *S. beurmanni* is the most frequently met with. It has been found in many localities. Description of the parasite, parasitology, etiology, pathogenesis and diagnosis.—B.M.J. ii./12,290.

Spotted Fever of the Rocky Mountains resembles symptomatically typhus exanthematicus. Supervenes on the bite of a tick *Dermacentor venustus*.—Manson.

Potent immune serum against Rocky Mountain spotted fever can be produced in the rabbit. 16 Cc. confers immunity to an average adult.—Hideyo Noguchi, per J1. Trop. Med., May 1/23, 145.

Remarkable variation in case-mortality. In Montana fatalities are 90% of the case-incidence, while in Idaho they are only 5%. Serum effective in reducing death-rate.—L. ii./28,473.

Sprue and Hill Diarrhoea—Features are sore tongue, stomatitis, a peculiar form of diarrhoea, due to varieties of bacteria. Milk diet recommended. Trilactine (g.v.) should prove of value.

In the endemic areas of the disease there is an excessive proteid diet or a diet containing an excess of fat. Excess of proteids stimulates over-production of acids in the gastric juice; the entrance of acid into the duodenum stimulates production of secretin, which leads to over-stimulation of the pancreas and an upset in the balance of other endocrine glands, including the parathyroids, thus causing disturbance of calcium metabolism. The "ionic" calcium of the blood becomes deficient in cases where chronic toxæmia is present, and in the author's opinion this is what occurs in sprue. Combined treatment with Parathyroid and Calcium has been found to give good results.—H. Harold Scott, L. ii./23,877.

In eight cases of severe anæmia associated with the sprue syndrome the micro-organism *Monilia psilosis* was isolated.—Na., 114, '24,657. *Monilia psilosis* vaccines of value. When used in addition to diet, the outstanding symptoms of sprue have disappeared in two-thirds the time required by diet alone.—J1. A.M.A. ii./25,849.

Etiology *Monilia* in tonguescrapings.—Ashford, Int. Conf. Trop. An., '24,693.

Liver diet, as used in pernicious anæmia good. In Ceylon liver soup is an old native remedy for sprue and it has long been recommended in the London School of Tropical Medicine.—Jl. A.M.A., ii./28,1039.

Staphylococci.

S. pyogenes Aurcus.—A spherical coccus about $0.9\ \mu$ in diameter, growing irregularly in clusters or masses. It is Gram+ and grows rapidly in all ordinary media at room temperature, though much more rapidly at body temperature. On agar a stroke culture is at first yellow, and then bright orange. It liquefies Gelatin.

S. pyogenes albus.—Similar to the above, but cultures are white. It has not been found possible to change one organism into the other.

S. pyogenes citreus.—Less frequently met with and differs in colour of cultures, these being lemon yellow. It is usually far less virulent than the two above.

S. cereus albus and *S. cereus flavus* are wax-like on Gelatin. Growth does not liquefy Gelatin.—M. & R.

Of all non-sporing bacteria staphylococci are the most resistant to desiccation, heat and germicides.—Stitt.

Streptococci.

Streptococcus pyogenes.—Occurs in chains, the cocci being slightly larger than Staphylococci ($1\ \mu$ in diameter). The distinction, *Strepto longus* and *S. brevis*, has been made as referring to the length of chains. Involution forms are seen in cultures, some of the cocci being as much as double size. The organism is Gram +. It grows more slowly than the Staphylococcus and dies out more readily. It ferments Lactose, Saccharose and Salicin, and usually has a strong hæmolytic action (on blood agar). In broth, the species producing the longest chains grow most distinctly in form of spherical granules—producing short chains giving rise to a finer deposit. The name, *S. conglomeratus*, is given to the variety forming distinct spherules of minute size.

A streptococcus does not necessarily explain an infection. Virulent forms tend to appear in long chains. Hæmolysis and action on carbohydrates of great value in differentiation.—Stitt.

Varieties.—Previously, *S. erysipclatis* was regarded as distinct from *S. pyogenes*. This is no longer held. Some have divided Streptococci according to length of chains and pathogenicity, but pathogenicity and morphology cannot be taken as a means of differentiation. Growth conditions, hæmolytic and ferment activity, and solubility or non-solubility in Bile Salts have to be taken into account in addition.

Fermentation.—Mervyn Gordon introduced nine tests. (1) Clotting of milk; (2) Reduction of Neutral Red; (3) to (9) Fermentation, with acid production, of Saccharose, Lactose, Raffinose, Inulin, Salicin, Coniferin and Mannite. By means of these Andrewes and Horder defined six varieties, five of which occur in the human being: (a) *S. mitis* in saliva and fæces as a saprophyte; (b) *S. pyogenes* as above described; (c) *S. salivarius*, corresponding to *S. brevis* of the mouth. As regards fermentation, this seems to bear the same relation to the next variety as *S. mitis* to *S. pyogenes*. It ferments Saccharose, Lactose, Raffinose, sometimes the Glucosides, rarely inulin. It clots milk and reduces Neutral Red; (d) *S. anginosus* equivalent to the so-called *S. scarlatinæ* and *S. conglomeratus*. It ferments Saccharose, Lactose, sometimes Raffinose, reduces Neutral Red, is actively hæmolytic; clots milk usually and does not grow on Gelatin at 20°C. ; (e) *S. fæcalis*, a short-chained form abounding in the intestine. Ferments actively and reacts to all the Gordon Tests except Raffinose and Inulin. It forms H_2S and does not hæmolyse blood; (f) *S. equinus*, common in the air and dust and appears to be derived from horse-dung.

The chief features of the three most important pathogenic Streptococci are, according to Gordon:—

	Neutral Red.	Raffinose.	Mannite.
<i>S. pyogenes</i>	—	—	?
<i>S. Salivarius</i>	+	+	—
<i>S. fæcalis</i>	+	—	+

Hæmolysis.—The medium used by Schotmüller is two parts human blood (or rabbit) and five parts melted agar, but 5 to 10% of blood is better. *Morphology of the Streptococci from lesions in the human subject* have hæmolytic action but occasionally Streptococci without the property are found—even in severe cases.

As to relation of Streptococci with *Scarlet Fever*, no definite opinion can be given. They are almost invariably present in the fauces and many of the complications of the disease are due to them. *S. anginosus* (*conglomeratus*) is specially abundant as a rule, though it also occurs in other acute catarrhal states. Gordon found, indeed, that the types of Streptococci in the throat in scarlet fever correspond with those met with in normal conditions. Maitland has isolated an organism named by him *Diplococcus scarlatinæ*, found in 80% of cases of scarlet fever, an oval coccus usually in pairs, like the pneumococcus and as it is soluble in Bile Salts and ferments Inulin is rather to be classed with that organism.—From M. & R.

ENTEROCOCCUS.—A lanceolate Diplococcus (+ Gram staining) was thought to be associated with trench fever in the war. It was present in 18% of the urines examined and in 16% of the blood specimens, and in 41% of infected wounds. The organism is a constant inhabitant of the normal bowel. It is remarkably resistant to heat. An emulsion in broth will stand 1½ hours at 55° C. This forms the basis for isolating the organism (1 hour at the temperature in question for emulsions of material—pus, fæces or sputum in broth with subsequent plating out of loopfuls on Conradi-Drigalski medium). Grows on all laboratory media both aerobic and anaerobic. Vaccines 2½ millions or less used as a diagnostic method. The effect of inoculations enabled investigators to determine whether the *enterococcus* was the infecting organism. Therapeutic dose, 1 to 20 millions.—T. Houston & J. M. McCloy, L. ii./16,632. *Still says it may be reported as a pneumococcus.*

R. Donaldson found it frequently associated with morbid processes especially intestinal. Often found during or after typhoid infections. Non-motile. Gram + Diplococci or in short chains. Resemble pneumococci in suggestion of a capsule. Pleomorphic according to time of growth on glycerin agar etc. Cultural characters with sugar reactions described. It is probably only a variant of the *Strepto-fæcalis* group.—B.M.J. i./17, 188.

Bacterial infection of telephones. Hæmolytic streptococci isolated in 15.9%, diphtheria bacilli in 2% and pneumonia bacilli in 1%, from transmitters and receivers of 94 telephones. Telephones should be sterilised.—C. C. Saelhof, per Jl. Trop. Med., Oct. 16/22, 329.

See also **Septicæmia** Vaccine Chapter. Vol. I. p. 928.

Neutral Red Egg Medium for cultivation of Staphylococci, see **Culture Media**.

Syphilis.—**Spiro-nema Pallidum.** *Syn. Spirochæta Pallida. Treponema Pallidum.*

Spiro-nema Pallidum was cultivated by Noguchi. Absolute anaerobiosis is necessary.

Serum water, to which a piece of sterile rabbit tissue (preferably kidney or testicle) has been added, is inoculated from the artificially infected testicular tissue of the rabbit (not from human lesions). The Serum (in test tubes) is rendered suitable for anaerobic cultivation by a layer of Paraffin Oil poured upon its surface. After the first cultivation strict anaerobiosis is not essential—the organism can be subcultured on to solid media such as gelatin or agar. The first growths are usually contaminated by other bacteria. Two methods are suggested for separating these from the Spirochæta:—(1) To grow the Spirochetes through filters which retard the passage of other organisms, or (2) a method depending on the fact that in stab cultures the Spirochetes grow away from the line of puncture into the surrounding medium, while other bacteria fail to do so. Noguchi states that Spirochetes cultivated by these methods are pathogenic in so far that after inoculation into the rabbit's testicle they produce characteristic histological changes and are found growing freely in the infected tissue.—H. Noguchi.—Jl. A. M. A., July 8, 1911, per L. ii./11, 536. B.M.J.E.ii./11, 48.

Noguchi's discovery of the Spirilla in the cortex cerebri of general paralysis.—B.M.J.i./13, 464; ii./13, 44.

Sp. pallidum has been transmitted from the brain of general paralytics to the rabbit by prolonged course of injections. Symptoms similar to those of

general paralysis in man have been produced and the blood gave a positive Wassermann reaction.—B.M.J. ii./13,1100, cf. also **Relapsing Fever**.

Alive may well be seen by parabolic or dark ground illumination, *vide infra*. Dead by mixing film with liquid Indian Ink.—*vide Burri's Ink, infra*. The use of **Collargol** is **satisfactory**.

Demonstration: As they chiefly infest the lymph stream, the spirilla may be obtained by "needling" base of ulcer or adjacent enlarged gland. Make film, fix in warm air, and stain 12 hours by Giemsa's Solution at 37° C. They are obtained only with difficulty from surface of ulcer.

Characters.—Gram negative. Smaller than *Sp. foetida*: regular and symmetrical corkscrew spirals, shorter than *Sp. buccalis*, greater number of turns. *Vide infra* for differentiation from other *spirochetes*.

Life Cycle of the Organism.

McDonagh regards the long incubation period of syphilis as due to the cycle of changes which the organism must undergo before it can give rise to symptoms, and puts forward in explanation that one dose of Salvarsan, though it kills every spirochete in a chancre, does not cure syphilis—the reason being that other forms of the parasite are present which are not killed by Salvarsan. The *Spirochaeta pallida* is never seen to divide, though present in enormous numbers in syphilitic lesions; this fact suggested that it was the end formed—the male sexual cycle. McDonagh states:—The commencement of the cycle is with a sporozoite or infective granule which by its mobility reaches and enters a cell, usually a mono-nuclear leucocyte. The sporozoite in some cases increases in size inside the cell in other cases it divides—where there is no division, the development goes on until spirochetes are formed—the male sexual cycle. In the case where there is division, one half runs the course of the male sexual cycle, whilst the other runs the course of the female sexual cycle, the latter at this stage seeming to leave the lymphocyte. The act of fertilisation was not seen: the result of fertilisation is the production of a zygote within which by subdivision sporozoites are formed and ultimately set free to start the sexual cycles again. McDonagh classes this organism with the sporozoa, and suggests that the parasite is a leucocytozoon, which should be called the leucocytozoon syphilis. The infection is probably conveyed by the sporozoite and not by the *Spirochaeta Pallida*.—P.R.S.M., Nov., 1912; P.J. ii./12,809. See also L. ii./12,1011,1178,1650; Pr., Dec., 1912.

The syphilitic spore has been shown to differ chemically from all the other phases met with in the life cycle of the '*Leucocytozoon Syphilides*.'—B.M.J. i./13,1611.

D'Este Emery holds, however, that *Sp. Pallidum* remains a spirochete throughout its life cycle.—L. i./14,222.

Directions for taking Specimens from a Chancre.—*Sv. Pallidum* are most abundant in the margin and in the deeper layers of the base of a chancre. The specimen should contain a minimum of blood cells.—J. H. Mills, L. ii./16,952. See further, p. 576.

Giemsa's Stain.

The following data are from Muir & Ritchie's "Manual of Bacteriology," 4th edn. (Second impression, 1921), p. 112.

"Giemsa believes that the reddish-blue hue characteristic of the Romanowsky Stain is due to the formation of methyl-azure, and he has prepared this by a method of his own under the name Azur I. From this by the addition of an equal part of medicinal methylene blue, he prepares what he calls Azur II. and from this again by the addition of eosin he prepares Azur II-Eosin. The formula for the finished stain is as follows:—

Azur II-Eosin 3 Gm., Azur II. 6·8 Gm., Glycerin 250 Gm., Methyl Alcohol 50 Gm.

The stain has been extensively used for demonstrating spirochetes, but can be used for any other purpose to which the Romanowsky stains are applicable. For spirochetes the following are Giemsa's directions:—

1. Fix films in Absolute Alcohol for 15 to 20 minutes. Dry with filter paper.
2. Dilute stain with distilled water—one or 2 drops of stain to 1 Cc. water (the mixture being well shaken).
(Sometimes the water is made alkaline by the addition of one drop of 1 per cent. Potassium Carbonate to 10 Cc. of water.)

3. Stain for 15 minutes (a longer period is often desirable, even 12 or 24 hours).

4. Wash in brisk stream of distilled water.

5. Drain with filter paper, dry and mount."

The method of procedure develops into either a long or rapid method:—

(1) *The ordinary or long method* consists in staining for 12 hours with 1:10 or 1:15 dilution.

(2) *The rapid method.* The same dilution is used but the slide with stain above is held over a Bunsen burner until steam rises. The process is repeated 3 or 4 times, the final application lasting 2 minutes."

The *long method* is recommended by the Medical Research Committee Report No. 19, issued 1918.

The method for the preparation of Azur 1 is kept secret, but in our 17th Edition, page 512, we described a process for polychroming Methylene Blue by treatment with ammonia, to give a Methylene Azure with similar uses.

Polychrome Methylene Blue may be prepared by heating 100 Cc. of 1% Methylene Blue solution with 20—30 mgm. of Sodium Peroxide for 15 minutes at 100°, and subsequently neutralising with Hydrochloric Acid.—J.C.S. Ai./25. 597.

The following simplifies matters:—

Some years ago we had occasion to experiment, and found that ordinary good medicinal Methylene Blue and Eosin will produce a suitable stain, the most satisfactory formula being:—

Eosin 0.4 Gm.

Methylene Blue medicinal 0.3 Gm.

Glycerin 50 Gm.

Methylic Alcohol, Acetone-free (not exceeding 0.3%), 50 Gm.

This solution was found by our pathologist to give good results with spirochetes. In the course of the work we determined that the "Acetone-free" requirement for the Methyl Alcohol is not entirely a fetish. Using a commercial Methyl Alcohol containing 12% Acetone the staining was not so good. The presence of Glycerin was also found to be essential.

Azur II. in the U.S. IX. was described as a mixture of equal parts of the Chlorides of Methylene Blue and Methylene Azur (Methylene Blue Sulphonate).

Long and diligent search is necessary in looking for *Spirochaeta* stained by this method. It imparts to the spirochete a distinctly reddish violet tinge, similar to that of the neighbouring leucocyte nuclei (the Romanowsky chromatin stain), whilst the bacteria come out blue.

Examination of Unstained Specimens.

The old methods of examining the spirochaeta in the hanging drop, and by staining with Giemsa's Stain have been completely superseded by the **Dark-ground illumination**, the **Chinese Ink** and **Collargol methods**.

Ultramicroscope.—Employed for demonstrating in a rapid, easy and certain manner the presence of the living organism. Useful to examine a scraping when it is necessary to give an opinion on a doubtful primary or secondary syphilitic lesion. Syphilis cannot of course be excluded because the organism cannot be detected on one examination.

The **Ultramicroscope** is a paraboloidal immersion-condenser. The rays of light used are deflected so that they converge obliquely on the object examined, which appears as a bright refractive body on a dark background. Transparent objects otherwise invisible are then easily seen.

Spirochæta pallidum seen thus is an extremely fine silvery spiral from 6-15 μ in length, with very regular or closely set spirals (about 7 to the diameter of a red blood corpuscle). The spirals vary from 10-26 in number. Extremities are pointed. If so focussed that only the summits of the spirals are illuminated the organism looks like a series of bright dots, not unlike a chain of Streptococci. It is feebly motile, its movements consisting of rotations round its long axis, backward and forward movements, and bending movements, which are the most marked. It preserves its spiral form during rest.

The technique of dark ground illumination is ably dealt with by J. Edwin Barnard, Pres. Roy. Microscopical Socy. in Med. Res. Com. Rep. No. 19, issued 1918.

Sp. pallidum. Method of demonstrating, using dark ground illumination with oil done away with. An ordinary achromatic condenser used dry with Travis' expanding stop replaces.—A. C. Coles, B.M.J. ii./15,777.

Sp. buccalis, *Sp. refringens*, *Sp. balanitidis* are much larger with wider and more open spirals. *Sp. refringens* has only 3 to 5 turns and is usually blunt at either or both ends. The only spirochaetes very like the specific organisms are (1), *Sp. dentium*, found in carious teeth, which is shorter (5 to 10 μ) and coarser, 5 to 15 spirals, the wave length the same as *Sp. pallidum*, but depth of wave is considerably less; (2), *Sp. pertenuis* (yaws), Castellani; (3), *Sp. pseudo-pallida*, Loewenthal (ulcerated cancers). In the last two the spirals are not quite so deep or regular, and in the case of *Spirochaeta pertenuis* the ends are often twisted into rings or loops.

Spirochaeta Pallidum is found below the surface in the lymph only and should be sought at the margin of the lesion. It cannot be detected in the centre of an ulcerated or necrosed area where the saprophytic spirochetes may be seen in large numbers. The organism is found in the largest numbers in mucous plaques, is constantly present in varying numbers in primary untreated chancres, and is usually detected in the papular syphilide and in scrapings from a recently removed enlarged syphilitic lymphatic gland.

The margin of the chancre, papules, or mucous plaque should be gently scraped till blood just begins to exude. The surface is now dried with a swab of plain sterile gauze, and then a little blood or serum expressed by decompression or by bandage. A small drop of this is removed with a platinum needle and mixed with a drop of distilled water on a thin glass-slide. A thin cover-glass is now pressed down firmly, so that only a thin layer of fluid remains between the slide and cover-glass. A drop of immersion oil is placed below the slide and on the cover-glass. The condenser must first be accurately centred. This can easily be done with a low objective (1 in. or $\frac{3}{4}$ in.) by means of concentric rings scratched on the surface of the condenser.

Any artificial light can be used—electric (arc or Nernst), gas (incandescent), or even an oil lamp. Concentrate the light to the centre of the microscope mirror. After the slide has been placed in position so that there is a layer of oil between the ultra-microscope and the under surface of slide, and after the object is focussed, the ultra-microscope must be racked up or down and the mirror adjusted till bright illumination with dark back-ground is obtained.

General or local treatment has a marked effect on the number of treponemata found, and the organisms tend to disappear after a few weeks from the site of the primary inoculation, even without treatment. Antiseptics must not have been previously applied to the sore.

Indian Ink Method (Burri).—The method is known in Germany as Tusche Verfahren.

The method requires no special apparatus. A platinum loopful of secretion from a sore is placed on a slide and mixed with an equal quantity of Distilled Water and an emulsion of Indian Ink. The whole is mixed and spread on the slide like a blood film, allowed to dry and examined with oil immersion lens. The ink produces a dark background and the objects stand out white. It is easy to differentiate the two forms of spirochetes.

Good scheme of examination for treponemes (using Indian Ink and dark ground illumination, also for gonococci using Methylene Blue). For treatment (syphilis) Lambkin's Cream. Pil. Hyd. c. Cret., Salvarsan, etc. For gonorrhoea Rogers' 20 oz. cholera irrigator and Permanganate 1 in 5,000.—E. T. Burke, Pr., July, 1920, p. 55.

Permanent staining of spirochaetes.—Annual Report of the Com. of the Privy Council for Medical Research, 1922-3.

The Indian Ink Method affords no information regarding the structure of the organisms apart from the arrangement of the spiral turns and shape and size of body. The Giemsa (using wet fixed films) is best.—Wenyon, 1934.

Collargol Solution 1 in 20 (store in Amber bottle) preferable to Indian ink. One drop with one drop of the suspected secretion to be mixed together, and allowed to dry on slide, and then spread with another slide to make a thin film. The preparation is examined with $\frac{1}{12}$ inch oil immersion lens—the background is perfectly homogeneous.—L. W. Harrison, B.M.J. ii/12, 547.

Or proceed as follows.—Make a thin film, fix by radiant heat. Pour the collargol Solution over film, decant quickly and stand up to dry in air or incubator. Examine with $\frac{1}{12}$ inch immersion lens.—Wyatt Wingrave.

Comparison with other Spirochetes.—

Sp. Refringens under dark-ground illumination is seen to shoot rapidly backwards and forwards in a straight line and when not rotating so actively

is often seen to squirm its way by corkscrew movements, pushing blood corpuscles, bacilli, etc., aside. Serum obtained by swabbing is preferable for examinations to scrapings. Stitt says: "While the rotary movement of *Sp. Pallidum* is rapid, it does not move across the field with the speed of other spirochetes. Thus *Sp. Refringens*—commonly present in genital ulceration—quickly traverses the field and shows more widely separated spirals. The *pallidum* shows a continuity of its spirals while in motion, but when at rest often shows the appearance of a series of silvery dots or dashes. Many individuals show a bend in the long axis."

In staining with *Giemsa's Stain* (diluted 1 in 8) at least 12 hours is best. In the *Indian Ink* method at least twice the volume of Indian Ink to the drop of serum. Spirochetes are more constantly present in condylomata and mucous patches and far less constantly present in papular secondary skin eruptions than in primary sores. *Dark Ground Illumination* is the best method.—B.M.J. ii./11, 1283."

Gentian Violet staining of *Sp. Pallidum*.—

The stain is prepared on the lines of Gram's Aniline-Violet for bacteria:—
Shake 3 Cc. Aniline Oil with 20 Cc. distilled water for 5 or 10 minutes, and to the filtered liquid add half its volume of a concentrated alcoholic solution of Gentian Violet. Fix smears by holding over 1% Osmic Acid Solution for one to two minutes. Pour the Stain over the specimen and heat 20 to 30 seconds over a flame. Wash off with water, dry and examine with oil immersion lens. Spirochetes appear reddish-blue against a rose-colored ground—*Sp. Refringens* being stained more deeply.—L.i./11, 321.

A simple method of staining spirochetes. Suspected materials spread on cover slides, free from all traces of fat, and fixed by 2% solution of Formaldehyde, containing 1% Acetic Acid, for 2 to 4 minutes. Wash with Alcohol 95% and treat with saturated aqueous solution of Picric Acid. After 10 minutes wash in running water and stain with Carbol Gentian Violet or Ziehl's Fuchsin Solution, when treponema are stained either violet or red, according to stain. Fuchsin gives more permanent stain, but violet colouration renders organisms more distinctive.—E. Renaux, C.D., Sept. 29/23, 435.

Lead Subacetate Method—Fix with Osmic Acid as above, wash in water and cover for 10 seconds with a solution consisting of Liquor Plumbi Subacetatis 1, Water to 100. Again wash and cover 10 seconds with 10% Aqueous Sodium Sulphide Solution. Wash and repeat whole process twice. Apply Osmic Acid Solution 30 seconds, wash and dry. Spirochetes cell debris and bacteria appear black.—A. A. W. Ghoreyeb. Publication of Mass. Gen. Hosp. vol. III., No. 2, p. 367, JI. A.M.A. May 7, 1910, p. L.i./11, 321

Silver Method (Tribondeau).—Use material from infiltrated tissue around chancre, not from surface. Eliminate hæmoglobin, etc., as far as possible by washing (*v. infra*). The *fixative* used consists of Formalin 2 Gm. Acetic Acid (Pure) 1 Gm., Water 100 Cc. The *Mordant* is 5% Tannin in Water. The Silver Stain is Silver Nitrate 1 Gm., in Water 20 Cc. To 15 Cc. of this add Ammonia drop by drop until precipitate redissolves; then add the remaining 5 Cc. of Silver Nitrate Solution until the solution remains slightly opaque after shaking.

Technique.—Dry smear at 37° C. Fix by washing with fixative one minute and complete by a few drops of Absolute Alcohol, allowing same to dry on the inclined slide. Add the Mordant and warm over flame till just steaming for 30 seconds. Wash, pour off excess and without drying employ the Silver Stain over a flame for thirty seconds. Wash and dry. *Sp. Refringens* and *Balanitidis* are darker and distinguished by their morphological character.—B.M.J.E. i./13, 16. See also Med. Res. Com. Rept., No. 19 issued 1918. The method is very similar to Van Ermengem's process for flagella—one cannot be certain of getting results every time.—W. D'Este Emery. Pr Feb., 1913, 462.

Fontana's Silver Impregnation Method.

- (a) Fixing Fluid:—Acetic Acid 1 Cc., Formalin 20 Cc., Water 100 Cc.
- (b) Mordant:—5% Tannin in a 1% aqueous Phenol solution.
- (c) Silver Solution:—Silver Nitrate $\frac{1}{2}$ % in Distilled Water. In use, a minute quantity of Ammonia is added until there is a distinct turbidity (avoid excess).

Dried films (not fixed by heat) are fixed in (a) 1 minute, the fluid being dropped on and renewed once or twice. The preparation is then washed

thoroughly, solution (b) is dropped on the film, heated until stain rises and allowed to remain about $\frac{1}{2}$ minute. Again wash in water, drop on solution (c), heat as before and allow to remain about $\frac{1}{2}$ minute. Finally wash and dry. Spirochetes are dark brown or black, and are easily found. This is a good method.—M. & R. It is almost identical with the preceding.

Congo Red—stained films acidified with dilute Hydrochloric Acid as relief medium for bacteria and spirochetes.

A small drop of 2% Aqueous Congo Red Solution is placed on the slide and a very small quantity of the bacterial culture or of the exudate to be examined is mixed with it. The drop is then spread out into a tolerably thick film. Allow to dry and wash the slide with 1% Hydrochloric Acid in Absolute Alcohol and dry in the air, or films may be spread and stained afterwards and treated with acid. Examine with oil immersion lens. The background will appear as a rule uniform. Bacteria vary somewhat in relation to the dye. Mostly they are clear, sharp and quite transparent, but some will take up the dye and appear as ill-defined bluish-black bodies—this is seen chiefly in old cultures of Gram negative organisms.—T.H. C. Benians, B.M.J. ii./16,722.

An atlas of 38 plates of Spirochetes was issued as a memorial of the late Fritz Schaudinn.

Noguchi's Method of Diagnosis of Syphilis.—(*Distinguish from the Noguchi modified Wassermann.*) Boil two parts of the cerebro-spinal fluid with 5 parts of a 10% solution of Butyric Acid in normal saline for a few seconds, then add one part of Normal Sodium Hydrate and again boil briefly. A flocculent or granular precipitate is obtained on standing (in parasyphilitic infections) due to presence of a globulin. The test distinguishes general paralysis from other forms of insanity not associated with meningo-encephalitis.

Complement-Deviation Reaction for the Diagnosis of Syphilis (Wassermann, Neisser and Bruck.)

To take blood for Wassermann Test.—A test-tube is provided with a cork drilled with two holes. Into the one is fitted a 2-inch length of glass tubing to which the needle for venipuncture is attached by a 6-inch length of india-rubber tubing. The other hole is merely to allow for the escape of air while the blood is flowing into the test-tube when the vein is punctured. The sterile test-tube should be moist inside (steamed). Venipuncture is best (1) because it provides practice in puncturing a vein, (2) ample serum is thus provided for one or more modifications of the test.—Claude H. Mills, L. ii./16,954.

The Pathological Section of the Royal Society of Medicine in 1914 and the Special Committee upon the Standardisation of Pathological Methods agreed that for the Wassermann Test:

(1) The ingredients (Red Corpuscles, Antigen, Hæmolytic Amboceptor, Complement) are to be derived from *different* sources.

(2) The serum to be tested is to be inactivated before use. An independent "hæmolytic system" is to be employed consisting of red corpuscles, an inactivated hæmolytic serum, and a fresh normal serum containing complement. The hæmolytic values of the antiserum and complement are determined by a separate preliminary experiment. As the test is a quantitative reaction the titre of the reagents ought to be known.

Unanimity is wanted in the detail of conducting the test. Some prefer the use of guinea pig serum obtained on the day of the test, while others say it should stand for 17 or 18 hours. Many find the advantage in adding Cholesterol to the Antigen, while others fear this addition may exceptionally produce non-specific reactions and so on. A positive reaction is evidence of extreme height.—Leader, L. i./18,641.

Standardised antigen and amboceptor and adoption of standard method for all approved laboratories.—B.M.J. i./19,344. See also W. D'E. Emery, L. ii./18,547.

The reaction was elaborated by Wassermann on the principle of the Bordet-Gengou reaction (1901). The Bordet-Gengou reaction is that which occurs when antigen, specific antibody and complement are exhibited together. As Wassermann was not able to use a culture of the *S. Pallidum* he made use of an extract of syphilitic *fœtal tissue* rich in spirochaeta. Subsequent work showed,

however, that the reaction was not a true Bordet-Gengou reaction, was not truly specific, and did not depend on an interaction between the spirochetes and a specific anti-spirochetal antibody, but was due to an altered condition in the serum of a patient during the active stage of infection, whereby, on the addition of various lipoidal substances an alteration occurred which caused complement to be interfered with in its activity. Modifications using 'antigen' extracted from normal organs are now employed to a large extent. For the reaction are required:

(1) **Antigen**, which is usually an alcoholic extract of normal heart to which some Cholesterin has been added.

(2) **A haemolytic system**, usually anti-sheep, requiring sheep's red cells and rabbit serum from a rabbit immunised against sheep's red cells.

(3) **Complement** obtained in guinea-pig serum.

(4) **Serum of patient and controls** of normal and syphilitic sera. These sera should be inactivated at 54–56° C. before use.

The only reliable test is when the constituents for the reaction have all been derived from separate sources and can be accurately standardised. The so-called rapid clinical methods are valueless.

Washed Sheep Corpuscles are prepared from the fresh blood by removing fibrin by clotting—rapidly stirring at the time of drawing from the animal. Centrifugalise with a powerful centrifuge and pipette off the Serum. Add Normal Saline Solution and again centrifugalise several times and finally dilute with Normal Saline Solution making approximately a 10% suspension of the corpuscles.

Wassermann's (original) test.—For a good description see B.M.J. ii./12, 1504.

For a number of other references dating from 1909 see Edn. XVIII, Vol. II, p. 556-558.

Parasyphilitic Conditions in Relation to the Reaction.

The 'W.R.' in blood and spinal fluid is often valuable in confirming a diagnosis of early tabes, but as a guide to progress and further treatment it is unreliable, and one frequently finds actively progressing tabes with a history of syphilitic infection despite a negative reaction in both blood and fluid.—C. P. Symonds, "Modern Tech. in Treatment," Vol. II., p. 40.—The Lancet Offices, London.

General paralytics give positive results in every case,—tabetics do not give it in more than 60%.—B.M.J. i./09, 1238; ii./09, 984; L. i./09, 1457, 1512.

Differential diagnosis of syphilis and parasyphilis of the nervous system. Practically every case of general paralysis gives a positive lymphocyte and a positive Wassermann reaction.—F. W. Mott, B.M.J. ii./11, 1337; L. ii./11, 1392.

Syphilis of the nervous system. The cerebro-spinal fluid of 127 cases of varied forms of insanity examined. 64 of these were general paralysis, and in 59 or 92.1% a positive result was obtained. 21 of the 59 since dead from general paralysis.—Mott, P.R.S.M., Neurol. Sectn., Feb. '10, p. 35 *et seq.*

The spirochete of syphilis, it is stated, actually flourishes in the brain in general paralysis and is present in, at least, some cases of locomotor ataxia.

Mental Disease, 150 cases.—In a number of cases of general paralysis the blood and cerebro-spinal fluid may give a negative Wassermann reaction even on repeated examinations. This does not agree with McIntosh and Filde's statement that "a negative reaction in serum in a suspected case of general paralysis will render this diagnosis improbable"; and "a negative reaction in the cerebro-spinal fluid of a general paralytic is unusual." A negative Wassermann reaction is more likely to be obtained in the case of a female general paralytic than of a male. The blood is negative rather more often than the cerebro-spinal fluid in the case of male patients, but the reverse obtains in the case of female patients. At least 0.1 Cc. of serum should be used for the test, and, where practicable, 0.2 Cc. should also be used. At least 0.5 Cc. of cerebro-spinal fluid must be used, if possible also 0.8 Cc. otherwise positive results may be missed. Practically the original Wassermann Test employed.—David Nabarro, B.M.J. ii./12, 1454.

Routine cerebro-spinal fluid examination in diagnosis of nervous disease. Cell counts, Protein content, Wassermann Reaction, Colloidal Gold Test.—A. Douglas Bigland, L.ii./20, 687.

CEREBRAL SYPHILIS.—A definitely positive W.R. indicates infection—a negative result is not always of value. In tabes, a negative reaction in the blood is by no means uncommon during a quiescent phase; even in the spinal fluid, the reaction is sometimes negative. In cerebral syphilis, when the

disease is progressive, a + W.R. in the blood can almost always be got. In the cerebro-spinal fluid the reaction may be + or —.—G. Riddoch, L. ii./23,3. According to McDonagh the reaction is positive in 40% of primary cases, 77% of untreated secondary cases, and 70% of tertiary cases.

Noguchi gives the following figures as indicating the percentage of positive W.R.' as determined by various serologists:—Primary syphilis, 69.8; secondary syphilis, 89.4; tertiary syph., 78.1; hereditary syph., 94.5; cerebro-spinal syph., 47.6; general paresis, 88.1; tabes 62.66. With cerebrospinal fluid general paresis gave 90, tabes 56.2 and cerebrospinal syph. 19.

The results obtained by different workers in different laboratories are fairly uniform, and the 'W.R.' is the most important single evidence of syphilis.—Stitt.

Lange's Colloidal Gold Test see Cerebro-Spinal Fluid Examination, p. 409.

General References to the Reaction.

B.M.A. (1910) DISCUSSION ON COMPLEMENT DEVIATION METHODS IN DIAGNOSIS, Prof. Wassermann's paper—B.M.J. ii./10,323,1427.

Useful in determining the specific nature of atypical lesions,—e.g., apparently non-syphilitic soft sores, of extragenital sores and of manifestations of the disease where primary and secondary symptoms had been suppressed. As a means of diagnosis the reaction is supplementary to the examination for spirochetes, and where these are scanty, as in tertiary lesions, it is available alone.—L. ii./10,1491.

In 5 cases of phthisis the only sign of syphilis was a + reaction discovered after death. At the necropsy the condition of the lung was suggestive of old syphilis. This seemed to support the view that syphilis affecting the lungs predisposes to phthisis. Post-mortem examinations in general give a correct diagnosis in non-syphilitic cases. As a rule if the reaction is + during life a syphilitic area will be found post-mortem.—B.M.J.E. ii./10,20, q.v., for further data on these lines.

The fallacy of the Wassermann Reaction is that when it ceases to be positive in the secondary stage it does not signify that the syphilis is cured, but only that *Sp. Pallida* has retired from the blood, into the tissues from which they may merge later and give rise to fresh symptoms.—L. ii./13,1225.

Significance of the Wassermann Reaction in gynaecological practice. In gynaecological ailments, especially those associated with uterine hæmorrhage, syphilis, it is stated, is very frequently present. Whenever there is metro-rhagia or menorrhagia apart from obvious cause, such as tumour, syphilis should then be suspected.—B.M.J. ii./13,1003.

Prostitutes—104 girls aged 14 to 18—half of whom resided in the poorest quarters, while the other half lived in the best districts,—all showed a + Wassermann reaction. Apart possibly from a certain proportion of congenital cases infection must have taken place recently and, therefore, all must have been in a highly infective state. Syphilis and the health of the community.—C. H. Browning, B.M.J. i./14,77.

Blood of 491 healthy persons examined. 46 or 9.36% gave a positive reaction. Prevalence of venereal disease indicated seems higher than might have been expected.—Sir John Collie, B.M.J. i./16,346.

Method of procedure for large number of tests.—P. Fildes and J. McIntosh, L. ii./16,751.

Surface Tension due to the alcohol used in making the Antigen thought to be the important factor in the Wassermann Reaction. The Alcohol itself is the Antigen.—V. B. Nesfield, L. i./17,18.

A quick method of performing with small quantities of serum.—F. E. Taylor, L. i./18,19.

Doubts as to value of the reaction. Because the Complement Deviation Test may be + it is inaccurate to say the case is syphilis.—A. S. Leyton, B.M.J. i./18,523.

Important principles connected with the Test. The addition of a little cholesterolin to the ox liver extract is important. The 'Standard Antigen' made up according to directions (L. ii./16,751) is now generally used. A dilution of 1 in 15 is found best.—J. MacIntosh, L. i./18,630,641.

Parenchymatous syphilis. Biological characters of *Sp. Pallidum*.—F. W. Cott, B.M.J. i./15,194.

Does a permanently negative serum reaction mean cure and a persistently positive reaction mean failure to cure and liability to late sequelæ?—J. Havelly Dick, Pr. June, 1920.

Rationale of Wasserman Reaction.—J. E. R. McDonagh, L.ii./21,1319.

Chemistry of Wassermann's Reaction. The bodies responsible for the + syphilis reactions are solely contained in the Englobin group of proteins. The hæmolytic bodies in hæmolytic amboceptor are chiefly contained in the pseudoglobulin group.—B.M.J E. ii./22,44.

The reaction only of value when interpreted in conjunction with other findings. A single negative of little value in presence of suggestive findings ; no evidence of cure.—R. A. Kilduffe, Jl. Trop. Med., April 2/23,118.

The reaction in the child at birth is in close agreement with that of the mother, but during the first few weeks of life the majority of children born with a positive reaction lose that reaction, and not only remain negative to Wassermann, but fail to develop clinical signs of syphilis during first 2 years. A positive reaction in new-born infants is therefore of no diagnostic value, and the incidence of congenital syphilis is much less than serological data indicate. High incidence of syphilis in adults due to either acquired, or, less probably, to late congenital syphilis. Effects of syphilis in mother chiefly seen in later months of pregnancy, leading to premature birth and premature still-birth. The diagnosis of syphilis in the new-born can be made definitely only after careful review of clinical, serological and pathological findings.—J. N. Cruickshank, Med. Res. Counc. Report on Maternal Syphilis, B.M.J. i./24,522.

Quantitative serum reaction for syphilis diagnosis.—G. Dreyer & H. K. Ward, L. i./21,956.

Serum diagnosis in Syria—an account of work undertaken to estimate value of serological tests in syphilis, tuberculosis, dysentery, typhoid and typhus. An analysis of 2,868 cases.—E. H. R. Altounyan, L. i./24,73.

Effect of malaria on the Reaction in syphilis.—Chronic malaria has no appreciable effect on the reaction. Acute malaria has the effect of increasing the anti-complementary powers of this serum. Pyrexia due to non-malarial infection has no effect on reaction.—E. H. R. Altounyan, L. i./24,73.

A positive 'W.R.' in the child at birth cannot be taken as an indication that the child is syphilitic. Over 90% of children born with a positive reaction lose it later.—J. N. Cruickshank, L. i./24,675.

The 'W.R.' remains for the present the best test for the detection of syphilis, though one or more of the flocculation tests may be done in addition. Kahn Test simple and apparently very serviceable. Probable that some form of flocculation test will eventually attain to extended use. R. B. Lloyd, I.M.G. Jan. '25,24.

Can it ever be said that a person who has had syphilis is cured? The 'W.R.' is insufficient evidence of cure. Infection can be spread in the tertiary stage.—P. N. Panton, L.i./26,763.

Interpretation of the Wassermann Reaction in adults.—T. E. Osmond, L. ii./29, 677.

Influence of Drugs on the Reaction.

Potassium Iodide and the early Arylarsonates (Atoxyl, Soamin and Orsudan seem to have little, if any, action on the reaction.

Mercury itself inhibits it.

Casoni took sixteen individuals, twelve of whom were definitely non-syphilitic, and four suffering from syphilis, and observed their reaction to the test before and after giving the following drugs: Iron Citrate, Sodium Arsenate, Strychnine, Guaiacol, Sodium Glycero-phosphate, and Quinine. In the twelve non-syphilitic cases the Wassermann reaction was negative both before and after treatment. In the four syphilitics one remained unaffected by treatment, the reaction being positive all the time. Of the remaining three, in one the reaction disappeared completely under arsenic, and in the other two it was much less marked. Quinine abolished it entirely in one, while it did not modify it in the others. It was only the quinine and arsenic which modified the reaction, and this not in every case. Iron, Strychnine, Guaiacol, and Glycero-phosphate had no effect.—B.M.J.E i./11,24

Subcutaneous injection of 1 mgr. Epinephrine Hydrochloride prevents reaction giving rise to a false "positive" 'W.R.'—Ind. Med. Res., July '25, per Jl. A.M.A., ii./25,1432.

Examination of Dried Serum.—The blood is collected in the usual way in a bent Wright's Tube, and allowed to coagulate. A definite quantity of the Serum is pipetted off and allowed to dry on blotting paper. This can then be treated with Normal Saline and made up to its original volume for conducting the test.

Sachs-Georgi Reaction.

Mix a 1 in 5 Alcoholic extract of heart muscle (beef, human, or guinea-pig), with 2 parts of Alcohol, and to 10 Cc. of this add 0.45 Cc. 1% Cholesterol solution. (The proportions may have to be varied.) Dilute with 5 parts normal Saline Solution, taking care that no precipitation occurs and that the dilution does not become cloudy. Inactivate patient's serum for $\frac{1}{2}$ hour in a water-bath at 55° C., and dilute with 9 parts normal Saline Solution. Place 1 Cc. of the diluted serum in a test tube and add 0.5 Cc. of the diluted antigen. As antigen control, mix 0.5 Cc. diluted antigen with 1 Cc. Normal Saline Solution (0.85%) and as serum control mix 1 Cc. diluted serum with 0.5 Cc. Normal Saline Solution and Alcohol mixed in the proportion of 5 to 1. A known positive and a known negative serum are used for control. Incubate test-tubes for 18—20 hours.

Interpret with an agglutinoscope after 18—24 hours. The antigen control should be absolutely clear and if the serum control shows any precipitation repeat the test. Distinct light particles against the dark background indicates positive reaction—negative sera are entirely clear or slightly opalescent. Strongly positive reactions show up within 2 or 3 hours in the incubator and can be read macroscopically.

Cerebro-spinal fluid should be used undiluted in 1 to 1.5 Cc. amounts.—Stitt, 250—252.

Meinicke's Third Modification of this test uses an Alcoholic, non-cholesterolised horse-heart extract for antigen.

Results closely approximate data got from Wassermann Reaction.—W. R. Logan, L. i./21,14.

Compared with Wassermann Tests.—T. Taniguchi & N. Yoshinare, B.M.J. i./21,239. See also P. Parthasarathy and co-workers, B.M.J. i./22,594.

Sigma (Σ) Reaction "S.R." (Dreyer & Ward, L. i./21,956). Said to be simple and accurate. Instead of five variables there are only two. An antigen which is a mixture of an Acetone-free Alcohol-soluble heart extract and Cholesterin is used. Flocculation after 9 hours at 37° C. is a + reaction.—A. F. Rook, L. i./22,118.

It is well worth while to use the Sigma Test and the 'W.R.' in conjunction, as neither singly gives a true result in every case.—J. Menton, Pr., Nov., '24, 379.

Apparatus for the Sigma Reaction.—J. W. Bigger, L. ii./24,742.

The "S.R." perhaps more sensitive than the various modifications of the 'W.R.' It is of high specificity and permits one to follow the results of treatment. Some factors influencing the flocculation methods of Dreyer-Ward and Sachs-Georgi.—I. R. Morch, L. ii./24,58.

Comparison of Sigma and Wassermann Reactions.—The S.R. appears to be of as great diagnostic value as the W.R. The technique of S.R. is simpler, but reading of results requires greater care and experience. In the study of syphilitics undergoing treatment S.R. is undoubtedly the method of choice. In serum diagnosis of syphilis, both methods should be used in elucidation of difficult cases.—E. H. R. Altounyan, L. i./24,73.

Sigma Reaction results.—P. H. Jones, B.M.J. i./25,821.

By means of the Sigma reaction it is possible to estimate with a high degree of accuracy the amount of reacting substance in the serum of cases of syphilis, the probable error of any single determination being about 6%, as compared with an average deviation in the case of the Wassermann reaction of 24%.—P. H. Jones, B.M.J. i./25,821.

Kahn Test.

To a 1 in 5 Alcoholic beef-heart extract add 4 mgr. Cholesterol to each Cc. a similar amount of extract being retained as a non-cholesterolised antigen control. Dilute the Alcoholic antigen with Normal Saline Solution (0.85%) in proportion of 1 to 2, and the Cholesterolised antigen in the proportion of 1 to 3. Pipette 1 Cc. Alcoholic antigen into a small test-tube, add 2 Cc. Salt Solution, and mix rapidly. The resultant opalescent mixture is ready for use. Dilute the Cholesterolised antigen similarly, using 3 Cc. Salt Solution; this has a tendency to precipitate, and is best kept in the incubator when not in use. Dilutions should be freshly made and not used until $\frac{1}{2}$ hour after dilution.

Place in each of 2 agglutination tubes 0.3 Cc. undiluted inactivated patient's serum. To the first tube add 0.05 Cc. diluted non-cholesterolised antigen, and to the second the same quantity diluted Cholesterolised antigen; agitate

vigorously. Strongly positive sera may show definite precipitation, particularly with the Cholesterolised antigen. To bring out precipitation in weaker sera place test-tubes overnight in incubator at 37° C. Read results next morning as follows:—(1) Precipitation consisting of one or more large clumps is denoted by + + + +; (2) a large flocculent precipitation by + + +; (3) moderate-sized flocculi or granules by + +; (4) small-sized flocculi or granules by +; (5) fine flocculi or granules by \pm ; (6) negative precipitation by —.—Stitt. (Some details have since been altered.)

A comparison of the Kahn and Wassermann Tests.—T. E. Osmond and D. McClean, B.M.J. i./24,617.

Wassermann, Sachs-Georgi and Khan Tests compared.—B.M.J.E. ii./24,16.

Review of recent diagnostic reactions.—Pres., July, '24,266. Sept., '26, p. 316-321.

Comparison of Kahn reaction with Wassermann Test in 29,000 cases showed that the Kahn Test gave fewer false reactions and consistently appeared more delicate, especially in early cases and cases following treatment.—Am Jl. Syph., per Jl. A.M.A. ii./25,65.

A series of 2,500 cases clinically free from syphilis gave 2,493 negative reactions by Kahn Test.—Per Jl. A.M.A. ii./25,1428.

Kahn Test gaining popularity. A more rapid and dependable test than the Wassermann; has replaced the latter in the Michigan Department of Health.—Jl. A.M.A. ii./25,1733.

Kahn Test superior to Wassermann.—U.S. Nav. Med. Bull., Nov., '25, per Jl. A.M.A. ii./25,1916.

Targowla Reaction.

This consists in mixing 15 drops of Elixir Paregoric (of Belg. Pharm., *i.e.* Tincture of Opium 50 Gm., Benzoic Acid 5 Gm., Camphor 3 Gm. Anethol 2 Gm., and 70% Spirit 940 Gm.) with 5 drops of Water and 15 drops cerebro-spinal fluid, while a control tube contains 20 drops of Water and 15 drops Elixir. A precipitate in 24 hours in the test is said to be given only in cerebro-spinal syphilis and disseminated sclerosis. A large number of cases have been tested. Not only is there a parallelism between this and the Wassermann, but the test appears to be more reliable in cases of cerebro-spinal syphilis, other than general paralysis or tabes.—L. ii./25,930.

Vernes Flocculation Test.

Depends on a flocculation reaction between the patient's serum and a special reagent, 'Perethynol,' prepared from horse-heart muscle by means of Ethylene Chloride and Alcohol. A suspension of the reagent in saline is flocculated in the presence of a syphilitic antibody and the degree of hæmolysis ascertained by a special photometer, the results being given quantitatively in definite figures. The only test officially recognised by the Municipality of Paris and the French Government. Individual error almost impossible. More mathematically accurate than either the Wassermann or the Sigma Tests.—Per Press Aug., '28,264; see also E. Offenheim, Pr., June, '28,376.

Description of a micro-precipitation test for syphilis.—M. G. Petermann per Pres., Aug., '28,263.

GENERAL REFERENCES TO SYPHILIS.

Royal Commission on Venereal Disease.

The paper deals with:—Syphilis of the innocent; is syphilis increasing? Modifications of syphilitic phenomena, notification and regulation, and the example of Australia.—Sir Malcolm Morris, L. i./13,1817. The danger of syphilis to the community and the question of State control.—H. C. French L. ii./13,990. Evidence by Sir V. Horsley and Dr. Florence Willey.—B.M.J. i./14,923.

Prevalence, Effects, Diagnosis and Treatment, Notification, Treatment by unqualified persons, Marriage and Communication of the disease. 10% of the whole population in large cities is affected with syphilis and the percentage with gonorrhœa must greatly exceed this.—B.M.J. i./16,346,380.

Sir William Osler's Lettsomian Oration of the Medical Society of London. Syphilis the despair of the statistician. No trustworthy data. Even in death a stigma is associated with it, and the returns were everywhere but under the special caption of the disease itself. In the case of the *Gonococcus* this organism is not a destroyer of life, but the greatest known preventer of life. Of 1,885 deaths stated to have been caused by syphilis in the Registrar

General's Report for 1915, 1162 were under 1 year, 1277 under 5 years. In 1915 of 800,000 children born 90,000 died within the first year. The number of these deaths from syphilis was probably between 15,000 and 20,000. Description of the Work of the National Council for combating Venereal Disease, 1914.—B.M.J. i./17,694.

Venereal disease in the Army. Sound advice. The work of the Association for Moral and Social Hygiene. The removal of prostitutes from areas of large camps.—L. i./16,305.

Antivenereal Campaign in Germany.

The German Society for combatting venereal diseases founded by Professor Blaschko and Neisser in 1902, has made enormous progress. Over six million warning leaflets suited to either sex have been issued by the Society, —they are designed to throw light on the hidden dangers of loose living. The information is compressed into ten short rules, which can be digested by the least intelligent and which are designed to contradict certain popular fallacies, as for example, that it is harmful to a man's health to abstain altogether from sexual intercourse.—B.M.J. ii./13,1174.

For brief details of the Venereal Disease Act, 1917, see Vol. I., p. 1022.

Combating venereal disease in Great Britain.—Col. L. W. Harrison, L.i./25,1216.

Syphilis did not exist in the Old World before 1493, but it existed in America before Columbus arrived, and his crew imported it into Europe.—Per Jl. A.M.A. ii./25,1514.

The possibility of an infection with syphilis taking place through the performance of a p.m. examination is an established fact and syphilis must now be included among the diseases with which pathologists may become infected.—Per Jl. A.M.A. ii./28,263.

Anaemia and other blood changes in syphilis.—C. L. Cummer, ii./28,689.

In Paris syphilis is on the increase. The number of cases, which fell regularly from 1920 to 1924, began to rise in 1925 and in 1927 was back to the 1920 figure.—L.ii./28,826.

Query's Serum.—*Dose.*—Injection, subcutaneously or intramuscularly of 25 ampoules, one a day for 25 consecutive days, ordinarily it is not necessary to renew the treatment. This preparation is made by immunising monkeys with a 'polymorphous bacterium' isolated from a syphilitic affection.

Relief of symptoms.—J. Dobriansky, J. H. Sequeira and T. Thompson, L. i./20,903. Two cases ineffective and 8 cases out of 9 (intramuscular use) improved.—B.M.J. ii./22,624,635.

Tick Fever.—Ross & Milne (1904), first showed the so-called African tick fever to be caused by a spirochete of closely similar character to that of relapsing fever, but bacteriologically it is more convenient to keep the two diseases separate,—associating tick fever with *Sp. Duttoni*. Dutton and Todd in the Congo Free State also Greig and Nabarro in Uganda, worked on the subject. Clinically the fever closely resembles relapsing fever, but the periods of fever are somewhat shorter—rarely lasting more than two or three days. The organisms are much fewer in the blood than in the European relapsing—fever. Morphologically they are almost the same.

The transmitting agent, *O. Moubata*, infests rest houses on the route of travel, hiding in the crevices of floors and walls and feeding at night. The female transmits the spirochete to its ova. Natives suffer severely in childhood, but develop immunity later.—Stitt.

Sp. Duttoni can be maintained virulent for wild mice in artificial media for 40 days. It will multiply and can be successfully transferred in artificial media—Egg Yolk in mouse decoction was the most successful medium.—L. i./09,834.

Through the bite of ticks from Nyassaland, collected in the hut of a native in whose house cases had occurred, Leishman was able to infect a monkey. The spirochetes appeared in the blood of the animal on the sixth day and it died on the thirteenth day. From the monkey, transmission had been possible to mice.—B.M.J. ii./08,1435.

Sp. Duttoni—the parasite of Tick Fever. Experimental investigation.—Sir W. B. Leishman, L.ii./20,1237.

Tick fever in America is synonymous with Texas fever and Rocky Mountain spotted fever, and the State of Montana (where, since 1914 spotted fever has occurred in 36 of 56 counties of the State) is attempting to get rid of the

ticks by means of a specially-bred tick parasite, 120,000 of which are liberated weekly between April and July. A prophylactic vaccine made from infected ticks is distributed free by the U.S. Public Health Service and is proving of value. (Jl. A.M.A. i./27,1649; i./28,1049.)

Trench Fever.

For a description of this war infection, with numerous references to literature see Edn. XVII., Vol. II., p. 529.

Trypanosomiasis (Sleeping Sickness).

The disease is endemic on the West Coast of Africa, notably in the Congo Basin, and is caused by the entrance into the blood and cerebro-spinal fluid of the parasite *Trypanosoma gambiense*. It causes a complete dislocation of the brain functions, slow inflammatory process goes on in the brain cells for years, gradually the individual becomes languid in the extreme, he has not physical energy enough to walk, speak, or even feed himself. The trypano- some of Gambia was first named and described by Dutton, who lost his life in 1905 in West Africa whilst engaged in his work on this disease.

The blood or cerebro-spinal fluid of an infected person has been injected into a monkey with result that the animal died with all the symptoms of sleeping sickness. In man it is transmitted from the sick to the healthy by a tsetse fly (usually *Glossina palpalis*). In the stomach of this fly the trypanosome multiplies by fission. A Scotsman, Alex. Maxwell Adams* (1901) first entertained the idea that sleeping sickness was caused by Trypanosomes.

The condition known as sleeping sickness may be regarded as the terminal stage of trypanosoma infections. The average duration is 4 to 8 months. Mania is not uncommon. Blood or gland-lymph examination, or if this be negative hepatic or spleen puncture should establish diagnosis. General paralysis of the insane, cerebral tumour, forms of meningitis have features in common. The Wassermann Reaction is of little avail as the sera of most cases give a positive reaction (Manson), but it is **absolutely reliable** as a **diagnostic test for dourine** of horses in Canada (a *T. Equiperdum* infection). By slaughtering all animals giving a positive reaction the disease has been almost stamped out.

Infection of man by *T. rhodesiense* was first recognised by Stephens and Fantham (1910). It is more serious than that caused by *T. gambiense*, running a course of only a few months and produces only exceptionally the symptoms of sleeping sickness as it is too rapidly fatal. Its distribution is very limited, viz., to the districts east and west of Lake Nyasa and it occurs in N. Rhodesia, Nyassaland, the south-east corner of Tanganyika Territory and the north-east part of Mozambika—Wenyon. For quite recent data see **International Conference and Commission, p. 588 et seq.**

Sir David Bruce classifies African Trypanosomes pathogenic to man and animals on morphology, pathogenic action on animals and mode of development in the insect host. With exception of *T. evansi* and *T. equiperdum* all are carried from sick to healthy animals by **tsetse flies**. The first of the three groups into which they are divided includes *T. brucei*, *T. gambiense*, *T. evansi*, and *T. equiperdum*. The second comprises *T. pecorum* and *T. simia*. The third embraces *T. vivax*, *T. capræ* and *T. uniforme* (*T. vivax*, *T. capræ*, and *T. uniforme* resemble one another closely, differing only in their average dimensions. It is questionable whether they are distinct species or merely varieties of *T. vivax*.—Wenyon, 565.)

The development of the first group begins in the intestines of the fly and ends in its salivary glands. In the second it begins in the gut and ends in

* Dr. Adams wrote us (Nov., 1921): In 1901 he certainly thought trypanosomiasis was nothing else than the old disease African lethargy, but it was not until Mar. 28, 1903, that he published in the B.M.J. his suggestion that trypanosomiasis was sleeping sickness, and that sleeping sickness was due to a trypanosome. Further, he first called attention to the possible association of *T. rhodesiense* with other species of *Glossina* (B.M.J., Apl. 16/1903, p. 889). *T. rhodesiense* is plentifully associated with *G. palpalis* in the Gambia. Both are capable of infecting man, the Rhodesian form is more lethal for animals; might we, therefore, have forms of a mixed infection present in man? There is certainly nothing to prevent this,—as seen in the case of malaria.—Further ref.: Jl. Roy. Microscop. Soc., June, 1903.

the proboscis. In the third the whole development is limited to the proboscis and does not occur at all in the intestines of the fly.—L. ii./14,1373; P.J. /15,33.

See also Croonian Lecture, L. i./15,1323 (a very concise account both of the Trypanosomes and Tsetse flies. In addition to *G. Morsitans*, the carrier of *T. brucei*, there are now some 13 different species. The antelopes on the shores of Lake Victoria act as a reservoir of the virus of sleeping sickness, hence the flies have retained their infectivity in spite of removal of the native population). L. ii./15,1 (Description of Nagana and differentiation of Nyasa- and sleeping sickness from that of the Congo. *T. brucei* is responsible for Nagana and *T. rhodesiense* is identical with it). L. ii./15,55 (Description of the Congo sleeping sickness). L. ii./15,109 (Description of *T. pecorum* and other types which so far as is known do not attack man).

See also Trypanosomes, Some remarks on Classification, by H. M. Woodcock, L. i./20,462.

If Tsetse flies were "successfully" introduced into India sleeping sickness might appear there in due course.—Manson.

Mott gave some analogies between **trypanosomiasis and syphilis**. Possibly the fashion in which the two organisms (*T. gambiense* and *Sp. Pallida*) originally invaded man was the same. *T. gambiense* can usually be found in the blood with ease, *Sp. Pallida* cannot, and seems able to multiply only in lymph spaces and channels. Possibly the deadly results of infection with *T. gambiense* as compared with other trypanosomes is due to *T. gambiense* having acquired the habit of migration into the subarachnoid space.

Spirochetes are generally believed to be linked to the protozoa rather than to bacteria. A Spirochætal invasion clinically differs from a bacterial one and conforms especially to certain trypanosome infections and there is great similarity of the histological lesions of the nerve tissues of chronic trypanosome infection,—e.g. sleeping sickness and the *mal de coit* (Dourine) of horses—to syphilitic and parasymphilitic lesions. There is further similarity in the fact that lymphocytes and plasma cells are found in the cerebro-spinal fluid in trypanosome diseases of animals and man, e.g., sleeping sickness.

Sp. Pallida though now transmitted direct from man to man was possibly at one time dependent upon a biting insect just as now is the Spirochete of tick fever.

One essential difference in effects on the nervous system between *T. gambiense* and *Sp. Pallida* is that whereas every case of this trypanosome infection leads finally to invasion of the nervous system, yet in syphilis not more than 5 or 10% even of untreated cases do this.

T. gambiense is the special organism of sleeping sickness whether acquired in the Congo State, or any other portion of Africa. Europeans are just as easily attacked as the natives. It is very doubtful whether the Organic Arsenic Compounds, Mercury, Trypan Red, etc., though causing the trypanosomes to disappear from the blood, will attack same when once in the cerebro-spinal fluid, as these drugs do not pass from the blood into the cerebro-spinal fluid. Various workers have suggested that the trypanosome may pass into latent endocellular form.

Some experiments on clearing the natives from the shores of Victoria Nyanza were thought to prove that *Glossina Palpalis* retained its infectivity for a period of two years, but there may be numerous means of re-infection of the flies.

Clinical Study and Pathological data of Human Trypanosomes, *vide* Mott. —P.R.S.M. Path. Sect. Nov. '10, p. 1, *et seq.* See also B.M.J. ii./17,104.

Sodium Arsanilate Treatment.—*Sudden or rapid death was frequently the termination of cases of sleeping sickness treated with full courses of this Organic Arsenical.*

Tryparsamide has been more successful.

There are indications that nature is working out a cure for herself by attenuating the virulence of the trypanosome, or by some other factor or combined factors.

Eighteenth Bulletin of the Sleeping Sickness Bureau.—It is suggested that *Glossina Morsitans* is harmless to man when occurring on open and relatively high ground, and probably dangerous in the presence of a sleeping sickness "reservoir" when inhabiting damp and warm valleys. Possibly the development of the trypanosome in the body of *Glossina*, which

in favourable circumstances is only in about 5% of these flies, does not occur in relative cold or dryness.—L. ii./10,323.

In the **20th Bulletin of the S.S. Bureau** records of 50 cases of Europeans are given,—of these thirty are known to be dead. One of the survivors, infected probably in 1900, is regarded as cured with Fowler's Solution.—Na Oct. 13/10,469. For more recent deaths, *vide References, postea*.

The staying of the disease in Uganda by clearing the Northern shores of Victoria Nyanza of its human inhabitants can only be temporary. The measure is not curative. It will be necessary to determine whether the animals in the district are capable of acting as hosts of the parasite.—B.M.J. i./11,82.

Experiments on eleven antelopes showed that after tsetse flies had been fed upon them, their blood eight days later transmitted the disease to all the monkeys inoculated, while two-thirds were infected after an interval of thirty days. The antelopes remained in perfect health, although in eight of them trypanosomes appeared in the blood for a few days only. No wild antelope inhabiting the Victoria Nyanza shore has yet been found to be naturally infected. Birds cannot act as a reservoir of the trypanosome.—Sir D. Bruce, Roy. Soc.'s Commission Report. Jan. 1911.

Wild Game & *T. Gambiense*.

There is little or no evidence to incriminate wild game as reservoirs of this trypanosome. Though it undoubtedly originated from a trypanosome of animals (probably *T. brucei*) it has now become adapted to man to such an extent that there is little tendency for it to infect game.—Wenyon, 539.

Trypanosoma lewisi,—the common rat trypanosome, is akin to the Trypanosome of sleeping sickness.

Infection with this trypanosome is now known to take place by uninfected rats eating the defæca of fleas, or the fleas themselves previously fed on infected rats. Yamasaki (1924) claims that the dog flea is able to infect by its bite by regurgitation from the stomach.—Wenyon, 469.

T. evansi causes the disease surra in elephants, camels, horses, etc., in India and Africa. The carrier of surra has not yet been identified. There are no tsetse flies in India. Details of differences between *T. evansi* and *T. brucei* are given.—Sir D. Bruce, Roy. Soc. per Na. June 15, 1911, p. 539. See also abstract of this authority's lectures at commencement of this chapter.

T. Cruzi. First discovered by Chagas in 1907 at Minas in Brazil, and since found to occur in other parts of Brazil and in Venezuela and Peru. Causes a form of trypanosomiasis often termed **Chagas' Disease**, occurring in children, but assuming an acute form in the first year of life. There is fever, and anæmia, and enlargement of liver and spleen and lymphatic glands, especially the thyroid. May occur in adults. Reduviid bugs are the transmitting host. The armadillo is a reservoir host. Wenyon, 488, *et seq.*

T. grayi identified with the crocodile trypanosome, *T. kochi*, infection of the crocodile taking place through its mouth, the incubation period being 4 days. The correct name of the Crocodile trypanosome is *T. grayi*. Monitors found not to harbour trypanosomes.—C. A. Hoare, Trans. Roy. Soc. Trop. Med., 25th June, 1929, 54.

A large number of older abstracts have now been removed.—See *Edn. XVIII., Vol. II., p. 564, et seq.*

International Conference on Sleeping Sickness.

Held in London, May, 1925, under the Chairmanship of Mr. Ormsby-Gore, Under Secretary of State for the Colonies, the other British representatives being Dr. Andrew Balfour and Dr. A. G. Bagshawe, together with representatives from France, Italy, Belgium, Portugal and Spain. Mr. ORMSBY-GORE said that the most important problems at the moment were administrative. In Central Africa, native social life was so intimately bound up with the keeping of cattle and other domestic stock that the problem of sleeping sickness could not be dissociated from that of animal trypanosomiasis (nagana). Inquirers were always brought back to the physical and administrative problem of the control and eventual extermination

of the tsetse fly itself. The task was tremendous, but there was hope.

The Conference made a series of recommendations, the most important being that an International Commission be set up to investigate certain problems in Equatorial Africa, such as the existence of human immunity, and the comparative value of trypanocidal agents, the part played by animals as breeding places, the relation between trypanosomiasis due to *T. gambiense* and *T. rhodesiense* respectively and the effect of precipitins applied to the blood in the alimentary canal of the tsetse fly. Uganda and the neighbourhood of Lake Victoria were considered the most suitable areas for study, and the local work should be presided over by Dr. H. L. Duke (Bacteriologist to the Uganda Govt.). The Commission should include a biochemist and entomologist and Dr. Kleine was invited to collaborate, the Commission to meet at Entebbe at the end of 1925 or in January, 1926, and twelve months later to present a special report to the League of Nations. It was estimated that £10,000 would be required, the various Governments concerned to be asked to contribute to a common pool; also recommended that a credit balance for 1926 of £3,000 be obtained from the League of Nations.—B.M.J. i./25,977,1014,1048.

The Commission commenced operations at Entebbe early in 1926, and issued an Interim Report (C.H.536) on its activities. Few definite conclusions were reached but the lines of research contemplated promised results of considerable importance.—B.M.J. i./28,225.

Final Report of the League of Nations International Commission on Human Trypanosomiasis.

Different strains of *T. gambiense* show great differences in cyclical transmissibility by *G. palpalis*, and it is justifiable to infer that at any stage of infection of man by *T. gambiense* the transmissibility of the trypanosome by *G. palpalis* may be lost. Its transmissibility diminishes when the strain is introduced into a sheep or goat and after some months in these animals it loses its transmissibility altogether and it is improbable therefore that these animals play any important part as reservoirs of this trypanosome; calves also are a negligible factor. *T. gambiense* may lose its transmissibility quite suddenly on transfer from one host to another by cyclically infected *G. palpalis*. *T. rhodesiense* and *T. brucei* are the same species, and *T. rhodesiense* is the name given to strains of *T. brucei* that can utilise man as a host, the majority of strains of *T. brucei* being incapable of so doing. The selection is exercised by the trypanosome rather than by the mammalian host.

Human trypanosomiasis never spreads in the absence of Glossina and this is the only insect in which the trypanosomes are known to develop cyclically. The virulence of the strain appears to be entirely independent of its transmissibility. A consideration of the factors which may influence the transmissibility shows that of four possible explanations of inhibitory effect—the fly, the climate, the host, and the trypanosome itself—the transmissibility of a

trypanosome by a glossina is a function inherent in the trypanosome itself.—H. L. Duke.

The Formol-Gel test is unreliable, as there are several tropical diseases in addition to trypanosomiasis which give positive reactions.

Cultures of *T. gambiense*, *T. rhodesiense* and *T. brucei* obtained with Ponselle's Medium (*q.v.*), using the same Sodium Chloride concentration. Rabbit serum may be replaced by monkey serum for cultivation of pathogenic trypanosomes of African mammals. When inactivating the media for the cultivation of pathogenic trypanosomes in the higher mammals it is well to increase the temperature from 70° to 75°.

Trypanosomes cannot exist in a medium contaminated by bacteria. Efforts to obtain positive cultures from blood and cerebro-spinal fluid of little value as a diagnostic method. The Complement-Fixation test should furnish more fruitful results than the Precipitation test in identifying the blood found in the alimentary tract of glossinæ.—M. Maximo Prates.

A study of the pathological lesions found in *infected monkeys* showed three distinct pathogenic types as follows:

(1) Chronic manifestations with few trypanosomes, approaching in 4 to 8 weeks sclerotic and infiltrative lesions of hæmatopoietic organs, meningo-encephalitis, sclerosis of the myocardium, and cachetic phenomena predisposing to extraneous complications. This group characterises the pathogenic action of human trypanosomes of the *G. palpalis* regions.

(2) Rapid manifestations with few trypanosomes, approaching terminal lesions in 2 to 4 weeks, with hyperplastic and hæmorrhagic phenomena in the hæmatopoietic organs, myocarditis, serositis, and nephritis, the early passage of parasites into the cerebro-spinal fluid, and lesions in the choroid plexuses. This group characterises the pathogenic action of human and animal trypanosomes of the *G. morsitans* and *G. swynnertonii* regions.

(3) Irregular manifestations of intermediary type, reaching in 8 to 10 weeks or 8 to 14 months, lesions of the first or second type, and usually chronic lesions associated with rapid terminal lesions. This group characterises the pathogenic action of trypanosomes of animal origin of *G. palpalis* regions (Damba Island).

Trypanosomal myocarditis frequently causes death in inoculated monkeys due to massive deposits of trypanosomes in the myocardium. In view of the cardiac disturbances and sudden deaths in human infections due to *T. rhodesiense* it is extremely probable that in these forms the cardiac changes are very severe and sometimes more important than the changes in the nervous system.

The cerebro-spinal fluid is a defensive mechanism against the invasion of trypanosomes (from the choroid plexuses), until its albuminoid content is raised.—M. Peruzzi.

Epidemiology in the *G. palpalis* and *T. gambiense* areas. The endemic in the Semilki area is serious, the virus showing a tendency to spread, creating fresh foci in the *palpalis* distribution area. There is every likelihood that the endemic will spread beyond its present limits and that the virus, which is sometimes **Arsenic-fast**, may spread through neighbouring territories, the natives possessing no safeguards and being themselves the first to spread it owing to migratory habits and racial ties. The effects of chemical prophylaxis are thus checked, and will be until the movements of persons and traffic are supervised.

In the Upper Uele district (Belgian Congo) the efforts of the Medical Service during the past three years have been crowned with

success, and the disease is abating, the causes being complete census of the natives, chemical prophylaxis, creation of a road system, and the prohibition of certain areas. There is no likelihood of the disease spreading to any considerable extent in this area during the near future.

It seems that the "danger zones," the reservoirs of trypanosomes, are extremely small in area, and are easy to destroy. Endeavours should be made to discover these reservoirs.

With regard to therapeutics, Tryparsamide is remarkably efficacious and should be used systematically in all cases where possible: Sulphoxyl-Salvarsan and Bismuth-Tryparsamide of no practical value, and Bayer '205' should be reserved for Arsenic-fast cases and, provisionally, as a preventive for natives exposed to infection.—L. Van Hoof and H. L. Duke.

General recommendations for the control of sleeping sickness.

The movement of native should be controlled. This implies: a census; the use of an identity card and passport by each native; delimitation of areas, entry into and departure from which are contingent on possession by a native of a visa stating he is free from trypanosomiasis; legislation to give force to these regulations and the endowing of medical authorities with judiciary powers; an international agreement for the control of the disease on frontiers; the establishment of observation posts for examination and control of visas.

There should be compulsory treatment for infected natives. Heavily infected zones should be evacuated. Clearing measures are costly and of little permanent value; in *palpalis* regions they should be restricted to much-frequented places and must be thorough and well-maintained.—F. K. Kleine, L. Van Hoof, and H. L. Duke. Abstracted from the Tropical Diseases Bulletin, Oct., '28, pp. 759-781.

See also *Organic Antimony and Arsenic Compounds* (Vol. I.) for recent treatment and refs., e.g., pp. 159, 167, 206.

Trypanosoma Gambiense, Characters of.

As a means of differentiation, it is stated that *T. gambiense* is capable of affecting *G. palpalis* and only rarely *G. morsitans*, whereas the reverse is the case with *T. brucei* (*T. rhodesiense*), though in the blood of man the two trypanosomes resemble one another closely.—Wenyon, 455.

Morphology.—On account of its scarcity in the blood of man, its morphology has been studied chiefly in the blood of animals, e.g., guinea-pig and rat. Its length is between 15 and 30 μ . There are various forms—a short and broad which has no flagellum, a long thin form with flagellum and an intermediate form. The short are the result of division of the long ones and they grow into long forms which divide (Robertson, 1912). Longer forms than above mentioned may be seen up to 40 μ . Macfie (1913) pointed to a stumpy form as a distinct species *T. nigeriense*,—probably merely a strain.

The nucleus is central and the kinetoplast a point a short distance from the posterior end. Undulating membranes are of moderate width and not greatly convoluted. Granules of volutin may or may not be present in the cytoplasm.

Trypanosomes in the cerebro-spinal fluid (in the later stages of the disease) show marked want of uniformity in size and shape—involution forms of no special significance.—Wenyon.

Staining is best conducted with **Leishman's Stain**, *q.v.*; some beautiful specimens can be made with this by first pouring on to the film and allowing to stain half a minute, then add twice the volume of distilled water and allow

to stain further half an hour. Wash in distilled water and dry in customary manner.

Other methods of staining are with Thionin Blue, Methylene Blue, Giemsa's Stain and Borrel's Blue, *q.v.*

Manson recommended the examination of the blood when the temperature is high; it is well to centrifugalise as the trypanosomes accumulate in the leucocyte layer above the red corpuscles.

Laveran's Method of Staining Trypanosoma.

Prepare thin blood films, and fix in absolute alcohol 5 to 10 minutes. The following are required:—

(1) *Solution*.—Methylene Blue and Silver Oxide (Borrel's Blue). Prepare "some" Silver Oxide freshly by means of Silver Nitrate and Sodium Hydroxide. Wash the precipitate with distilled water thoroughly, and add to it a saturated solution of medicinal Methylene Blue. Allow to remain for a fortnight, occasionally shaking.

(2) Aqueous Solution of Eosin, 1 per 1,000.

(3) Solution of Tannin 5%, or, better, a solution of 'Tannin Orange.'

Mix just before use: No. 1 Solution 1 Cc., No. 2 Solution 4 Cc., Distilled Water 6 Cc.

Stain in a flat dish, film downwards, for 5 to 20 minutes—5 to 10 minutes is enough in most cases. Wash in water and treat with tannin for a few minutes. Wash in water and then in distilled water. If precipitate found on the preparation wash in Clove Oil and brush off with Xylol.

References to Trypanosomiasis.

For older references see *Edn. XVIII.*

Sleeping sickness in the Belgian Congo. 45,000 patients treated over a period of three years. At first only Atoxyl was administered and complete cure was not effected under $2\frac{1}{2}$ to 3 months, but with the treatment of Atoxyl-emetic complete cure is never longer than $1\frac{1}{2}$ months.—J. Schwetz, *per Jl. Trop. Med.*, April 15/24,96.

Observations on transmission and prevention (in game-extirminated areas). Man seems to be the important reservoir. While it seems possible that *T. brucei* is capable of conversion into as train pathogenic to man, it seems unlikely that this often happens in nature.—*B.M.J. i./23,394.*

Bayer '205' is described, Vol. I., p. 314. Suggestions for its manufacture.—*B.M.J. i./24,413.*

Sleeping sickness in Africa. League of Nations Conference.—*L. i./25,1155.*

J. O. Shircore suggests the possibility in *T. rhodesiense* infection of an uninfected cerebro-spinal fluid becoming infected with trypanosomes from the blood carried by the needle in lumbar puncture, or by bleeding from the vessels of the spinal membranes damaged by passage of the needle, and further suggests that the blood should previously be cleared up by Bayer '205,' Atoxyl, or Tartar Emetic.—*Trans. Roy. Soc. Trop. Med.*, Feb., '28.

Lumbar puncture may be dangerous, especially if repeated, in patients with *T. rhodesiense* infection, not only from the likelihood that blood from vessels ruptured by the puncture may carry trypanosomes from the vessels into an uninfected cerebro-spinal fluid, but principally because the blood which escapes into the cerebro-spinal fluid may **increase the albumin content** of the latter sufficiently to allow of there surviving in it parasites which have reached it from the choroid plexus, which is actually the seat of the early invasion of trypanosomes. Further studies are necessary on the degree of persistence of albumin artificially introduced into the cerebro-spinal fluid and its influence on invasion of the parasites.—*M. Peruzzi, Trans. Roy. Soc. Trop. Med.*, June, '28,95.

T. brucei of Uganda is usually non-pathogenic to cattle of Uganda, and *T. vivax* usually has negligible pathogenicity, while *T. congolense* causes heavy death, but by passage mechanically from ox to ox it loses its virulence and becomes non-pathogenic. Transmission occurs readily in the absence of the tsetse fly. No satisfactory method of diagnosing chronic cases exists, yet it is believed that it is usually from the relapses of such animals that many outbreaks in Uganda arise. Tartar Emetic satisfactory in *T. Congolense* infection, but fails to cure in some cases and leaves 'premunized' animals

which may be the source of future outbreaks. No satisfactory treatment yet found for *T. vivax* infection.—U. F. Richardson (Uganda Vet. Service), Trans. Roy. Soc. Trop. Med., Aug., '28, 143.

In cattle harbouring *T. congolense* or *T. vivax* **Tartar Emetic** is of value—as many as 80% may be saved if treatment is commenced early, 1 Gm. being given intravenously every 5 days for 6 doses. Of no value in horses infected with *T. brucei*.—Wenyon, 462. Has proved successful in saving the lives of thousands of animals. A form of Antimony which can be injected subcutaneously is urgently required for practical reasons.—Ll. E. W. Bevan, Trans. Roy. Soc. Trop. Med., Aug., '28, 154.

Criticism of statement that 'no treatment has been found to give satisfactory results in the case of *T. vivax* infection' (in cattle). After a single course of Tartar Emetic injections relapses to *T. vivax* infection are the exception, whereas relapses to *T. congolense* infection are the rule.—H. E. Hornby, Trans. Roy. Soc. Trop. Med., 30 Jan., '29, 403: also J. N. Hall, *ibid*.

Though **Bayer '205'** caused rapid disappearance of the trypanosomes, the **nephritis**, and in some cases **amblyopia** progressing to complete amaurosis militated against its general employment.—Work of Sleeping Sickness Commission in Portuguese W. Africa in 1923, per T.D.B., Oct., '28, 784.

Tryparsamide.—In patients of the first stage, a total dosage of **20 to 40 Gm.** usually **suffices to produce a cure**, but in chronic cases 50 to 100 Gm. is necessary (Van den Branden). The best dosage for adult males and females in good condition is 3 Gm. weekly, and in poor condition 2 to 3 Gm.; for children 0.5 to 2 Gm. Action is rapid, durable, constant, and definitely superior to any other known drug, relapses or incomplete cures being due to extraneous causes; toxic reactions are negligible, cases of total blindness recorded being due to previous Arsenical treatment (Marugo). Treatment with Soamin and Tartar Emetic more prolonged and more uncertain than with Tryparsamide; in 25 out of 61 cases treated with the latter the spinal fluid became normal (Van den Branden). Of 100 cases treated all were cured, or in advanced cases the disease was completely arrested. Can be given either intravenously, intramuscularly, or subcutaneously. Quicker, easier, and less painful than Atoxyl, and the **most efficient drug so far available**. (Kellersberger). The single course of 50 Gm. for an adult appears to cure 52% and to ameliorate greatly 48% in the second stage. Accidents insignificant and ocular troubles rare and not severe (Infante). The drug is of great moral value to the natives 'who witness veritable resurrections,' and are beginning to have as much confidence in the treatment of sleeping sickness as they have in the treatment of yaws and syphilis (Trolli).—Abstracts of eight papers on the use of Tryparsamide, Ann. Soc. Belge de Med. Trop., per T.D.B., Oct., '28, 790–794.

Bayer '205.'—Given intrathecally, alarming symptoms may follow even small doses.—Per T.D.B., Oct., '28, 795.

'Tryponarsyl Meurice' is a Belgian product of the same chemical formula as Tryparsamide and having the same action on human trypanosomiasis.

Bacillus Tuberculosis.

Relationship between Human and other forms of Tuberculosis.

The Royal Commission on Human and Bovine Tuberculosis in its Reports (1907–1911) found that the human and bovine types are *morphologically indistinguishable*, but cultural characters of the organisms differ, also the pathogenic effects on different animals. The human types grow more luxuriantly, although Bovine Bacilli vary among themselves in luxuriance of growth. *Re* pathogenicity; only cattle, goats, pigs and rabbits are susceptible to the Bovine Bacillus but not to the human; guinea pigs and monkeys are susceptible to both types. Possibility of transmuting one type into the other cannot be denied, though experiments for the most part failed. Both types have been obtained in certain instances from the same patient. *The cultural differences are, however, not sufficient*

to establish the two as distinct organisms.* In a considerable proportion of cases of tuberculous disease in man the lesions are caused by bacilli in every respect indistinguishable from the bovine type.

Mammals and man can be reciprocally infected. Bovine animals are not completely immune to the human type, although they possess a high degree of resistance to it. The bovine has been found in man. The majority of human cases from which bovine bacilli were recovered were instances of tuberculous disease in children. *Infection by cow's milk, beef and pork is possible,—infants and young children are, therefore, specially endangered.* Even in adolescents and adults so large a proportion as 5 out of 55—the number investigated—showed the presence of the bovine type, thus indicating the same sources of infection as are possible at other periods of life. —B.M.J. ii./ii,122. L. ii./ii,166.

The fact is proved beyond question that tuberculous affection of the cervical glands and of the abdomen in young children is in a large number of cases set up by the bovine type. With regard to infectivity of milk the importance of dosage in the transmission of tuberculosis is brought out. The virulence of the subsequent infection is almost always in direct proportion to the size of the dose administered,—this doubtless accounts for the diminishing susceptibility of the human subject to the effects of the bovine type of disease as age advances,—B.M.J. ii./ii,180 (Leader). *Vide also* B.M.J. ii./ii,628,634. P.J. ii./ii,492.

Prof. Gosio, of Italy, endeavoured to upset the findings of the Royal Commission on Tuberculosis. He claims that where there is much tuberculosis in animals there is little in man and *per contra*, where there is much in man there is little or none in animals. Data are given showing that consumption of European cows' milk is associated with prevalence of tuberculosis in various countries, whilst, *e.g.*, in Morocco, where there are no European dairy cows, tuberculosis is unknown.—B.M.J. i./i3,96.

Infectivity of Tuberculosis.—Numerous criticisms of H. Batty Shaw's lecture on Pulmonary and other forms of Tuberculosis reported—L. i./20, Jan. 24, are answered by the lecturer—L. i./20, 517: "There are so many good arguments for the theory that the only infection with tubercle bacillus which really matters is the one contracted in childhood that one hesitates to be optimistic, as these critics are, that segregation will stamp out tuberculosis." One critic (O. M. Holden) goes so far as to prophesy that tuberculosis will in a generation be as uncommon as leprosy. As to cleaning up herds of infected cows the tuberculin test is not satisfactory. Cattle may be tuberculous and yet not give the tuberculin reaction.

Possible Test to distinguish Human and Bovine Types of Tubercle Bacillus.—The rabbit (synovial membrane of the knee joint) is injected with a bacillary emulsion (not mixed infection) or with pus or other pathogenic fluid. By the amount of reaction it is claimed possible to determine nature of infection, *i.e.*, if bovine the changes are rapid and acute, if human

*HISTORY OF TUBERCULOSIS. Schorstein Lecture (Tubercle bacillus discovered by Koch in 1882). It seems now to be established that Koch was right in stating that human and bovine tuberculosis are *not the same disease* and that there are pathogenic differences cannot be denied.—P. Kidd, B.M.J. ii./22,987.

the reaction is only slight. The distinction is stated to be clinically and pathologically most striking.—B.M.J. ii./12,1433.

A report on the results of a chemical investigation undertaken by Arthur Harden, F.R.S. (assisted by S. G. Walpole), at the request of the Royal Commission was published as Appendix, Vol. VI., of the final Report of the Commission. It contains a systematic quantitative comparison of the action of the two types, and shows that **no definite physiological difference** has been detected between the human and bovine types of tubercle bacilli. The report contains much bacteriological and chemical detail, and must be consulted by those requiring detail of the investigation.

INTERNATIONAL TUBERCULOSIS CONGRESS AT ROME.—B.M.J. i./12,903,950.

Infection of the human being by the tuberculous cow can and does occur. An answer to "Dangers of Sterilised Milk." by R. Mond.—L. i./14,145.

Portals of entry of the Tubercle Bacillus include, especially in childhood, the respiratory system, alimentary tract, mucous membrane of the nasopharynx, the skin and the placenta—antenatal infection.—Necessity of directing prophylaxis towards suppression of contamination from man to man and principally in the family. Bovine infection is of less frequency.—E. Emrys-Roberts, B.M.J. i./13,210.

Tuberculous Milk, Report on.—20% of samples examined were tuberculous.—B.M.J. ii./14,71. See also G. S. Elliston, B.M.J. i./21,174, and a Leader, "The Milk Supply," showing the unsatisfactory state of control.—B.M.J. i./21,236. **For T.B. in milk see also p. 467 et seq.**

Children and tuberculous milk. Attitude of public authorities—a good letter.—R. Stenhouse-Williams, L. ii./20,869.

Hereditary factor in tuberculosis.—Karl Pearson. L. ii./20,891.

The bovine type is distinctly **more susceptible** to the prejudicial effect of ordinary atmospheric influences (**daylight and drying**) than is the human type of tubercle bacillus. This difference between the types may in part explain why aerial infection with the bovine type is so infrequent in human beings.—L. Findlay & W. B. M. Martin, B.M.J. i./15,110.

HUMAN, BOVINE AND AVIAN TUBERCULOSIS DIFFERENTIATED. The human type is not confined to man or even to mammals, nor the avian type to birds, while the bovine occurs in a large variety of animals, not excepting man himself. The test for specific virulence is usually limited to inoculation of the rabbit. Occasional failure in the resisting power of these animals to human tubercle bacillus. Useful tables are provided showing *inter alia* susceptibility of various animals to infection with the three types. The fowl and other domestic birds are insusceptible to human and bovine bacilli. Spontaneous tuberculosis in the dog is relatively uncommon. This animal is difficult to infect artificially. Both mammalian types are capable of infecting dogs, but the avian type never. Of the deaths attributed to tuberculosis of all kinds about 6.5% are attributable to bovine bacilli and therefore to infection coming from the cow, probably in the immense majority of cases through milk.—L. Cobbett, L. i./22,979.

The figure for bovine infection in Manchester is 56%, the route of infection being as a rule via the digestive tract.—L. ii./21,1277.

Bone tuberculosis in children. Out of 150 cases 27% bovine type.—Sir H. Gauvain, B.M.J. ii./21,201.

Tubercle bacilli derived from sputum by cultivation. Of 212 cases of phthisis pulmonalis in England and Scotland, 205 were the standard human type, 4 were atypical human, and 3 standard bovine. Antiformin method used for obtaining cultures. No other investigator in this country has cultivated from tuberculous sputum any but tubercle bacilli of *human* type.—A. S. Griffith, L. i./16,721.

In England and Wales in 1909, 10,000 children under the age of 5 died from tuberculosis (other than pulmonary tuberculosis) and it is estimated that 70% of our dairy cattle are affected with tuberculosis.—B.M.J. i./13,96.

Tubercle-Immune Cattle—an attempt to breed, employing Kerry Cattle by crossing with Somerfords.—L. J. Picton, B.M.J. ii./18,157.

In New Zealand the control of Tuberculosis is facilitated by the fact that the percentage of animals affected is smaller than in this country, and secondly that tuberculosis had been scheduled as a contagious disease in New Zealand for a considerable number of years. Dairy cattle are under systematic examination both on import there and in use. Owners of infected

cattle are compelled to report suspected disease and compensation is granted for cattle condemned.

Upwards of 60% of milch cattle are tuberculous. Decreasing mortality from tuberculosis among adults probably largely due to increasing attention to general hygiene and cleanliness. A further possibility is that **ingestion of the organisms in milk during childhood** may assist in setting up and **increasing general resistance of body**. While adult tuberculosis rate is declining, consumption of milk is steadily increasing. Römer's law that where tuberculosis is rare it is acute and fatal, but where common it is chronic and relatively benign, is finding increasing support. What would be the state of this country if we eradicated tuberculosis without doing so in the rest of the world? Tubercle-free milk not desirable, if we could ensure regular optimum dose of bacilli. Danger from milk less due to presence of bacilli than to presence of excessive number of bacilli.—B.M.J. ii./24,676.

Prevention of bovine tuberculosis.—B.M.J. ii./24,1123.

It will be **impossible to rear cows** free from tuberculosis while their **resistance is lowered by constant milking** without any corresponding Vitamin 'A' addition to their food. The calves are generally fed on artificial foods, chiefly Linseed Oil, deficient in Vitamin 'A.'—M. J. Rowlands, L. i./25,1163.

Human bacilli produce: Pulmonary tuberculosis, tuberculous laryngitis, secondary intestinal ulceration, fistula in ano.

Bovine bacilli produce: Enlarged lymph glands, abdominal tuberculosis, lesions of bones and joints, meningitis, acute miliary tuberculosis, lupus, and rarely secondary extension to lungs.

The infections are antagonistic to each other and human and bovine bacilli are rarely found in the body at the same time. Practical measures are eradication of tuberculosis from dairy cows and pasteurisation of all milk for human consumption.—N. Raw, B.M.J. i./27,373.

Saliva of little importance in the spread of tuberculosis, tubercle bacilli being found in only 1.5% of fairly strong patients. Cough spray the most dangerous channel of infection, the bacilli being found in 50% of cases.—B.M.J. E. i./25,5.

The present position of the tuberculosis problem.—Sir A. Newsholme, L. i./26,1021.

A resumé of current literature on tuberculosis.—Pres., Aug., '27,271.

Role of monocyte in tuberculosis.—John Hopkins, Hosp. Bull., Oct., '25, per J1.A.M.A. ii./25,1754.

Tuberculosis in the Tropics.—The author stated he had never met a case of pulmonary tuberculosis in which he had been able to satisfy himself that any good had resulted from the administration of any form of **Tuberculin**, though he had seen many cases in which **chances of recovery were destroyed** by its use. Before clinical use is made of such a remedy, overwhelming evidence should first be produced that it confers immunity on animals. Diagnostic Tuberculin not now employed by Ministry of Health, owing to risk of revival of an apparently arrested or quiescent affection. '**Gigantic errors in diagnosis.**' Of 100 cases taken at random of soldiers pensioned for tuberculosis, one-third were proved by the Ministry of Pensions to be wrongly diagnosed. In 206 of a further 271 cases invalided for pulmonary tuberculosis, tubercle bacilli had never been found in the sputum, and only 22 of the cases on subsequent examination presented unequivocal evidence of the continued presence of pulmonary tuberculosis—that is, 249 cases cured out of 271, all due to sanatorium treatment! The finding of tubercle bacilli in the sputum the only *positive proof* of the presence of pulmonary tuberculosis. Tuberculosis problem, to a very large extent, a housing problem in all parts of the world, including the Tropics.—Sir James K. Fowler, Int. Conf. Trop. Am., '24,796-814.

From a study of the subject in Manchester not less than 25% of the tuberculous children under five years of age suffered from infection of bovine origin and this estimate is much lower than one based on probabilities would be.—Prof. S. Delépine, B.M.J. ii./12,1486.

Hamburger came to the conclusion that 95% of all the children in Vienna aged 15 are infected with tuberculosis, the infection being by aspiration from man to man.

Tuberculosis in infancy. An investigation into the conditions in

Edinburgh (371 cases) compared with results of Hamburger and others. Bovine infection in the Edinburgh cases have a considerable share in tubercle infection in that city.—B.M.J. ii./12,677.

Rainbearing Winds.—Prevalence of pulmonary tuberculosis increases considerably in districts exposed to strong Rainbearing Winds, *e.g.*, in those exposed to W., S.W. and N.W. winds. In these districts in England death rate is 1 per 1,000 *per annum*, and in districts sheltered from these winds the rate is nil. Pr., Jan., '13,300.

Wet Winds and early phthisis. As a result of an investigation extending over 25 years, a mass of diverse evidence has been collected, clearly pointing to one and the same thing, that prevalent, strong, rain-bearing winds exert a profound influence on phthisis, affecting both its incidence and course. The chance of becoming phthisical is at least twice as great in exposure to these winds as in shelter from them, while the chance of recovery is also twice as great when sheltered from them; there is therefore no detail of treatment more vitally important to the patient than the placing of him in effective shelter from these winds.—W. Gordon, B.M.J. ii./24,985.

Tuberculosis incidence and climate in India.—"The direction, steadiness and strength of the rain-bearing winds appear to be the most important factors, in addition to high rainfall and absolute humidity, in influencing the prevalence of pulmonary tuberculosis in Indian jails." Strong support of Dr. W. Gordon's (Exeter) views.—Sir L. Rogers, B.M.J. i./25,256-9.

Persons of gouty 'diathesis' or of gouty parentage show a marked resistance to tubercle.—H. E. Waller, Pres., Nov., 1913,298.

Tuberculosis in Dogs is comparatively rare—it is almost invariably due to infection from a human source. The symptoms—emaciation, loss of strength, etc., are easily recognised.—B.M.J. ii./13,827. On the other hand we read the prevalent opinion that dogs are practically immune to tuberculosis is erroneous. In three years 165 cases were recorded, all being verified anatomically and bacteriologically. The disease is more prevalent among dogs in town than in country districts. Cats also are capable of infection, but are less frequently affected than dogs. Horses seem to be very rarely affected, scarcely one, in 15,000 cases examined, has been recorded.—Cadiot, P.J. i./14,287.

Tuberculin.—Active principle isolated, it is said, at the University of Chicago. A crystalline, water-soluble protein of the nature of an albumin, formed directly by the tubercle bacillus, which is unstable and quickly becomes denatured. In view of this, the Tuberculin reaction may be interpreted as an allergic protein reaction.—Jl.A.M.A. ii./28,648.

Tuberculin Dispensary Treatment is dealt with in Vol. I., p. 944.

The following recent note may be given here:—

None but experts should give Tuberculin for diagnosis or treatment, and not even the best qualified medical practitioner should use it in treatment without at least three months' training at a Tuberculin Dispensary. Rather than waste money trying to teach ignorant people how to prevent tuberculosis it should be spent in educating medical men to recognise and treat the disease so as to prevent it becoming infectious. Tuberculin could reveal serious tuberculosis that could not be detected in any other way. In 1927 the Ministry of Health spent £3,150,000 in dealing with consumption. St. Pancras's share was £22,000, which allowed £10 for the treatment of each patient. At this cost, by Tuberculin Dispensary methods 5 to 10 times as many patients could be treated as sanatoria could treat, with better results—the patient could often go on working and providing for his family. Sanatorium treatment a curse to the taxpayer, the patient, and the sanatorium doctor. The scientific method has not had a fair trial in any country, because it is highly technical, difficult to learn, to teach, and to practise, and its evaluation demanded exacting conditions; leading men had rejected Koch's work and teaching because they have never seriously investigated it under these conditions. Wrong doses have been given in the wrong way at the wrong time, and in the wrong cases. Experiences at the Tuberculin Dispensary in London showed that in all patients in Stages I and II, where tubercle bacilli were found in the phlegm, 68% were alive at the end of 8 to 10 years, and 70% able to follow their ordinary occupations; the L.C.C. results in similar cases, under sanatorium treatment, were 28% alive at the end of four years. The advocacy of Tuberculin, both as a diagnostic and curative agent, rests on facts that can not be impeached.—W. Camac Wilkinson, B.M.J. ii./28,444.

Staining Methods for B. Tuberculosis :

Ziehl-Neelsen method ; Sputum and sections.—1. Prepare film from sputum or a section ready for staining, and fix by usual methods. 2. Heat filtered carbol-fuchsin in a test-tube and cover specimens with it entirely : stain films 5 mins., sections 10 mins. (**Carbol-Fuchsin Solution.** Neelsen's Solution, is prepared by mixing Concentrated Alcoholic Fuchsin *Solution 1 with 5% Carbolic Acid Solution 9, slightly warmed.) 3. Wash well in water. 4. Decolourise almost completely by immersing in 25% sulphuric acid. (If 3% Hydrochloric Acid in 95% Alcohol be used instead smegma and similar organisms are excluded). 5. Wash well in water. 6. Counterstain with

Alkaline Methylene Blue—sputum, 1 to 2 mins. ; sections, 3 to 4 mins. This stain is prepared by mixing saturated Alcoholic Methylene Blue Solution 142 mins., with 1 ounce of a 1 in 10,000 solution of Caustic Potash. (Note.—Medicinal Methylene Blue is far more soluble than ordinary and should be used.—W. H. M.)

Carbolised Methylene Blue is also employed :—Dissolve Methylene Blue 1 as much as possible in Alcohol 90% 7, and add Phenol Solution 5% 70, allow to settle and decant. 7. Wash, dry, and mount in Xylol Balsam (sputum). 8. If section dehydrate with alcohol, clarify with xylol, and mount in xylol balsam. If dehydrated with anilin oil instead of alcohol a clearer preparation is produced.

Examine wherever possible the first sputum expectorated after the night's sleep.

Fuchsin-Aniline Green Method.

Solution A. Fuchsin 10, Absolute Alcohol 100.

„ B. Strong Ammonia Solution, 3. Water 100.

„ C. Water 80, Nitric Acid 20, Malachite or Iodine or Acid Green 1 g.s. to saturate. Methyl Green does not give satisfactory results.

Add one part of A to 10 of B. Warm until vapour arises, immerse 1 minute, wash with water, then immerse in C 40 seconds. Wash off thoroughly. Bacilli red on pale green ground.

RECOGNITION.—Delicate, straight, or more usually slightly curved rods. When stained, usually beaded in appearance. The length of the organisms is commonly said to be about one-quarter to one-half the diameter of a red blood-corpuscle, but it varies considerably. Involution and branching forms occasionally met with. (Gram +).

The Tubercle Bacillus is about $1\ \mu$ in length when grown on Blood Serum and from 1.25 to $6.5\ \mu$ in the tissues.

Present in large numbers when the process is acute, but relatively scanty or absent in chronic forms of tuberculosis, e.g., caseous non-suppurating glands, lupus, &c.

Tubercle Bacilli contained in sputum retain their vitality for a considerable time even when the sputum dries up

The actual staining agent in the Ziehl-Neelsen technique is an additive product of the Phenol and basic dye employed.—B.C.A., Dec., '28, 1403.

Spengler's Method.—(1) Stain with Carbol Fuchsin steaming for 3–5 minutes, (2) Pour off Carbol-Fuchsin and apply Picric-Acid Alcohol (2 Gm. Picric Acid in 40 Cc. distilled water ; stand for 24 hours, filter and add equal vol. 96% Alcohol) for 2–3 seconds, (3) Apply 3–4 drops 15% Nitric Acid for 5 seconds, (4) Pour off and apply Picric-Acid Alcohol till sputum looks yellow, (5) Wash, dry and mount. Considered by many superior to all other methods.—Stitt.

To obtain satisfactory specimens of sputum.—Tubercle bacilli are often not found in sputum owing to bad specimens. An active cough reflex may be excited by sniffing vapour of essential oil of mustard from neck of bottle containing a small quantity. When this fails intralaryngeal injection by syringe of a few drops of a weak solution of Sodium Bicarbonate to which is added a little Hydrogen Peroxide ; or alternatively transnasal instillation of a few drops

* Distinguish Fuchsin from Acid Fuchsin, *Syn.* Fuchsin 'S,' Acid Magenta, a mixture of the Ammonium and Sodium Salts of trisulphonic acids of Rosaniline and para-Rosaniline. It is made by sulphonating Rosaniline Monohydrochloride (Fuchsin) with 'Oleum' and neutralising the sulphonic acids obtained. It is more soluble than ordinary Magenta. The formula of Sodium Acid Fuchsin is $C_{20}H_{16}N_2(SO_3Na)_3 \cdot H_2O$.

of the solution. The administration for a few days of Potassium Iodide also facilitates expulsion of sputum.—Sir J. Dundas Grant, B.M.J. i./28,628.

Rosolic Acid Method.—Specially for *B. Tuberculosis* in tissues. Stain in hot carbol fuchsin for 5 minutes. Wash quickly in tap water. Dip five or six times in saturated Alcoholic Solution of Rosolic Acid (Corallin) till fuchsin is removed. Wash in water and counter-stain in saturated Alcoholic Solution of Methylene Blue.

Konrich's Method. Stain with hot Carbol-Fuchsin for $\frac{1}{2}$ to 2 minutes, rinse with water, decolorise with 10% Sodium Sulphite solution for $\frac{1}{2}$ to 1 minute, rinse with water, then counter-stain with Malachite Green (50 Cc. of saturated aqueous solution of Malachite Green in 100 Cc. Distilled Water) for $\frac{1}{4}$ to 1 minute.—Y.B.P., 1922, 39,40.

Harrison's (L.E.) Stain consists of 1 Gm. basic Fuchsin added to 100 Cc. Distilled Water. To 75 Cc. of the filtrate is added 10 Cc. 37% Liquor Formaldehydi, 10 Cc. saturated aqueous solution of Phenol, and 5 Cc. Glycerol. Stains tubercle bacilli and Vincent's organisms a brownish-black against light yellow-brownish background. Gram-positive bacteria, the diphtheroid group, and spore forms, also stain well.—Jl. Lab. Clin. Med., per Jl. A.M.A. ii./25,636.

Cultivation.—*B. tuberculosis* was first grown on blood serum by Koch, but will not grow without addition of glycerin to the ordinary media. Requires temperature of 37° C. Dry wrinkled growth, somewhat like a lichen, on glycerin agar in three weeks. Cultures, especially in glycerinated broth, have fruity odour.

To obtain a pure culture of the organism from tubercular material it is necessary to inoculate guinea-pigs with same and after a lapse of four to six weeks cultures are made from enlarged glands direct on to blood serum or glycerin potato. Glycerin agar is not recommended for use direct *post mortem*, but the organism flourishes on this on sub-culture.

Change in the morphology and staining powers by growth on Spermin Oil and Glycerin-egg medium.—A. H. Miller, L. ii./14,739; i./15,704.

An acid medium apparently favours the growth of the tubercle bacillus, while an alkaline medium appears to be unfavourable. Steapsin or Lipase, alkalized and mixed with a strong cohydrolizer of wax, decorticates the tubercle bacillus, as does also a similar Insulin mixture. Further experiments in progress using Ozone and activated Oxygen as adjuncts. Also experiments in which tubercle bacilli, subjected to the decortivating action of Steapsin and Insulin with Chloroform as cohydrolizer, are being used as a bacterin.—Jl. Trop. Med., Dec. 15/24,348.

Sulphuric Acid-Crystal Violet-Potato Cultivation Method.—Take 1 Cc. of the specimen, whether sputum, urine, or tissues, beat to a homogeneous pulp and place in a 15 Cc. sterile centrifuge tube with 1 Cc. 6% Sulphuric Acid. Stopper with sterile cork and incubate at 37° C. for 30 minutes, shaking occasionally. Dilute contents with 10 Cc. sterile 0.9% Sodium Chloride solution, well mix and centrifugalise. Decant supernatant fluid and seed the residue on to the surface of the Crystal Violet-Potato medium. Cap culture tube with tin-foil after cotton plug has been impregnated with hot Paraffin. Prepare medium by cutting large clean peeled potatoes into cylinders 3 inches long and $\frac{5}{8}$ " in diameter. Halve cylinders longitudinally and soak immediately for 1 to 2 hours in 1% Sodium Carbonate solution containing 1 in 75,000 (0.0015%) Crystal Violet (mix just prior to use). Then gently wipe cylinders and place in sterile culture tube containing 1.5 Cc. 5% Glycerol broth cotton plugged, and sterilise in autoclave for 30 minutes. After incubation on this medium for 2 to 6 weeks a luxuriant elevated growth of tubercle bacilli becomes visible when positive. Equal in efficiency to the guinea-pig inoculation method and is recommended as a substitute for diagnostic purposes as it has many practical advantages. The medium found better than Dorset's Egg Medium and others, or favouring growth of Tubercle b. when present in small numbers.—H. J. Corper, Jl. A.M.A. ii./28,373.

Peptone Culture Medium for *B. Tuberculosis*.

The use of a medium consisting of the product of pancreatic digestion of beef, Glycerol, Dextrose and Salts, is advocated.—Ann. Institut. Past., '26, 746; B.C.A., '26, A1062.

To exclude Acid-fast Bacilli and all other Bacteria except Tubercle and Leprosy.

1. Wash film in Alcohol after fixing by radiant heat.
2. Stain with hot Carbol Fuchsin.

3. Differentiate in 25% Sulphuric Acid and wash freely in tap water and Alcohol.

4. Counterstain in Picric Acid and Alcoholic Solution. Dry and examine by 1/12th inch immersion lens.—Wyatt Wingrave.

POINTS OF DIFFERENCE BETWEEN HUMAN & BOVINE TUBERCLE BACILLI.

The Royal Commission on Tuberculosis found it impossible to differentiate between the human and bovine types of tubercle bacilli by means of staining methods.—Earlier data 17th Edn., p. 540.

Antiformin.—A Hypochlorite disinfectant. In 2 to 5% dilution kills most bacteria in 5 minutes. Anthrax Spores, require 10% for 12 hours. It does not, however, kill Tubercle bacilli (probably by reason of the fatty envelope which is believed to enclose them). It can be used to isolate the bacillus from the sputum—particles can be removed by macerating for 2 hours 20 to 30 Cc. of tuberculous sputum with 15 Cc. of Antiformin and diluting with water to 100 Cc. These inseminated on blood serum are stated to produce a pure culture—or may be used for staining direct.

May be made by passing Chlorine into 15% Sodium Hydroxide Solution to near saturation.—L. i./15,356. Other formulæ in 18th Edn., Vol. II., p. 573.

It dissolves hair, wool, silk, etc., also 0.5% is stated to dissolve Cholera Vibrios, Spirochetes, Trypanosomes in 5 minutes, while a 2.5 to 5% solution completely destroys vegetative forms of bacteria.

Loeffler's Modified Antiformin Method.—To 5 to 20 Cc. of sputum add equal volume of Antiformin 50% diluted with water. Heat until clear liquid results. To 10 Cc. of the mixture add 10% Solution of Chloroform in Alcohol (5 Cc. generally suffices). After shaking centrifugalise 15 minutes. An opaque layer is then formed between the Chloroform which occupies the bottom of the centrifuge and the supernatant fluid. Pipette off the latter and remove the opaque layer wholly on to a slide. Make films, fix and stain. This method is said to be rapid and simple and to give good results.—L. ii./11,1747

As used at the Lister Institute the sputum is mixed with an equal quantity of a 30% dilution of Antiformin, and the mixture incubated over-night at 37° C. After centrifugalising the fluid is poured off and replaced by an equal bulk of Normal Saline. After shaking up, again centrifugalise. Films from the deposit thus washed adhere better to the slide. Its use is justified by small percentage of 'corrections.'—B.M.J. ii./12,411

Cruickshank employs Antiformin for isolation of the bacillus, then inoculation of Glycerinated Egg Medium with centrifugalised sediment. The Bovine Bacillus grows best *without* Glycerin.—B.M.J. ii./12,1298.

Antiformin digestion of sputum, followed by centrifugalisation and examination of sediment, revealed tubercle bacilli, which could not be seen in the simple smear in 22 cases. Antiformin method more efficient by 9%.—Per Jl.A.M.A. ii./25,226.

Glycerin most useful for isolating acid-fast bacilli from contaminated material, e.g., Tubercle bacilli in tissues also in sputum preserved in glycerin remain alive for months, possibly years, in cold storage.—C. C. Twort, L. i./22,1221.

B. Tuberculosis in fæces. Formerly it was thought that the discovery of *B. tuberculosis* in fæces was diagnostic of tuberculous enteritis,—the bacillus, however, frequently occurs in fæces of patients suffering from pulmonary tuberculosis.

Acid-fast bacteria resist Antiformin when diluted to 20% for 2 to 5 hours—other bacteria and organic matter generally are speedily dissolved. A small piece of fæces (about a cubic 1/2 inch in size) is placed in a conical glass and to this some 20 Cc. of Antiformin diluted with Water to 15% is added and the whole well mixed. More of the diluted Antiformin is added and the mixture allowed to stand for about an hour. A white curdy precipitate appears on mixing and settles. Beneath this white layer some unchanged faecal matter remains and above the white layer the fluid is of a clear yellow or brownish color. A drop or two from the white curdy layer is mixed with a drop of Albumin Water and stained by the Ziehl Neelsen method. Much searching may be necessary. For certainty Alcohol may be used in addition to Acid for decolorising.—B.M.J. ii./19, 84; L. ii./10,1747. See also B.M.J.E. i./10,36.

Urine—At least six films should be prepared. The specimen is centrifuged, the supernatant liquor is poured off, and the sediment is washed two or three times by shaking up with sterile water, centrifuging on each occasion. Fix film with alcohol. Stain as for sputum, by Picric Acid method. Smegma B. is acid- but not acid- and alcohol-fast. Always wash film with albumen water before staining.

B. Tuberculosis in Pus.—Tubercle bacilli can be found microscopically in well over 90% of specimens of tuberculous pus from lesions of bones and joints. Half-saturated watery Picric Acid the best counter-stain—restores red colour to feebly acid-fast bacilli otherwise invisible or unrecognisable.—A. D. Gardner, L. i./26,1090.

Ligroin method of Detection:—To 5. Cc. of Sputum in a flask add 50 Cc. Caustic Potash Solution 5%. Shake and leave at room temperature until the sputum is homogenised. Dilute with 50 Cc. tap water and shake again. Add 2 Cc. Ligroin and shake until emulsion is formed. Warm to 60° C. until evidence of layer of smaller bubbles on the surface. A number of drops are then taken from immediately below this superficial layer and placed on a warm slide. The dry film is then fixed with Saturated Sublimite Solution and stained by Ziehl-Neelsen method—L. ii./10,1747. The Ligroin causes the Tubercle Bacilli to rise to the surface of the meeting of the two liquids.

Blood.—Tubercle Bacilli according to Leibermeister can be demonstrated in the blood in every case of open pulmonary tuberculosis, and in many cases of early disease.—B.M.J. i./23,1055.

Milk.—In spite of supervision it is no doubt true that a very large proportion of samples of milk supplied currently for human consumption are tuberculous. *For recent statement, see p. 483.* The staining is similar to that used for urine. Both the cream and the sediment must be carefully searched on centrifuging. It is well to soak the slides at the outset after drying and fixing, in ether for a minute or two to remove the fat. Stain by Picric Acid method to exclude butter bacilli. *Negative results in all instances are not necessarily conclusive of absence of infection.* Injection of susceptible animals is then necessary for confirmation.

Acid-Fast Bacteria. In addition to *B. tuberculosis*, *B. Leprae* (q.v.) and the *Smegma Bacillus* which resists acid by the Zeihl-Neelsen method the following organisms give identically similar reaction.

1. *Timothy Grass Bacillus*. Syn. *Moeller's Grass Bacillus* producing lesions closely resembling tubercles. Another variety of this organism has been found in the dust of hay lofts, and a third variety is known as the 'Mist bacillus' (Dung bacillus).

2. The *Petri-Rabinowitch Butter Bacillus* producing lesions closely allied to tuberculosis when injected into the peritoneal cavity of guinea-pigs.

Only in the case of material where outside contamination has been possible do these Bacilli '1' and '2' become an element for consideration—i.e., the customary method of examination is practically of unvarying value—Muir and Ritchie.

CHRONIC EAR DISCHARGES AND ATROPHIC RHINITIS.—Acid-fast organisms (but not alcohol-fast) present in every case of true atrophic rhinitis (ozæna) but in no other disease of the nose. Further work shows that a certain acid and alcohol-fast bacillus possessing close morphological and tinctorial resemblance to T. B. producing lesions undistinguishable from tuberculosis is present in every such case. To exclude tubercle other films in addition to the Z-N films are heatstained by carbol-fuchsin, then passed through the acid bath and washed freely in alcohol before counterstaining—preferably in saturated alcoholic picric acid. This proves them to be alcohol- as well as acid-fast; some of the special bacilli in question are only acid-fast. Some are, however, distinctly alcohol-fast. The Ziehl-Neelsen stain is only roughly diagnostic and not so precise as picro-fuchsin which emphatically excludes all bacilli which are only acid-fast.—W. Wyatt Wingrave.

Opsonins are substances contained in the serum or plasma of the blood and possess the power of influencing bacteria in such a way as to render them more easily attacked by phagocytes.

In addition there are said to be bodies variously named agglutinins, precipitins, lysins, and stimulins. To the last named Metchnikoff in particular attributed the power of stimulating the phagocytes to destroy invading organisms. This worker assigned to 'Opsonins' a secondary role.

The demonstration of the presence of some such body or bodies by comparing the phagocytosis occurring in (a) Bacterial Emulsion and washed corpuscles and in (b) Bacterial Emulsion *previously acted upon by Blood Serum* and corpuscles, is a comparatively simple and conclusive experiment proving its or their presence.

The action of Opsonins is, to a certain extent, independent of quantity, and they are decomposed by heating Serum at 60° C.: on the other hand in the dried condition they will withstand 120° C. Experiments show that there exists a **Preopsonin** which, when necessity arises yields the appropriate Opsonin for a given bacterium.

It is obviously necessary at the outset to determine the nature of the disease to be treated by the examination of the blood or pus.

The Opsonic Index for a given organism, *e.g.*, *B. tuberculosis*, is the ratio of the opsonic power of the serum of a patient compared with that of the normal being.

The Index as a means of diagnosis is not now employed to any extent except by some in tests of immunisation and determination of strain.

In the 16th edition, page 349, we gave details for collecting blood for determination of the Index and the conclusions to be drawn.

Complement Fixation Test in Tuberculosis.

One can, according to Wassermann and Bruck, determine, by means of the complement deviation, the presence of minute quantities of bacterial matter on the one hand and of corresponding antibodies on the other. Tuberculin is mixed with the serum of patients in graduated quantities and a small quantity of fresh normal guinea-pig serum, *i.e.*, complement-containing, is added to each of these mixtures. After an hour at 37° C. a specific hæmolytic serum previously inactivated by heat is added to each mixture, and then some red blood corpuscles towards which the serum possesses hæmolytic properties. (The hæmolytic power of the serum must naturally have been previously determined). If there are any specific Antibodies present in the serum to be examined, they will combine on the one hand with the Tuberculin, and the complement of the normal guinea-pig serum will become bound, hence there will be no hæmolysis as the hæmolysing power of the specific hæmolytic serum necessitates the co-operation of the free complement. Proper controls are necessary.

In this way the presence of Antituberculins in the blood of tuberculous patients, at least in such cases as had been treated with specific Tuberculin preparations, can be shown and the determination of the amount of anti-tuberculin in the patient's sera gives an index of the degree of immunisation, but the amount of specific immunising bodies will doubtless vary independently in the same way as do the Opsonins.

The directions in question should be read in conjunction with the criticism of D'Este Emery to the effect that Emulsion of killed Tubercle Bacilli was found better than Tuberculin as Antigen,—the Emulsion to be accurately standardised—*e.g.*, to 4% bacillary substance. The criterion as to the strength of the reaction is the time necessary for the complete absorption of all complement when the Serum and Emulsion are mixed in certain proportions (1:4) and incubated—using sensitised human corpuscles. In health the absorption time is 15 to 25 minutes—in 40 tuberculous cases under 2½ minutes. Prognosis is good when the serum contains a large amount of antibody and therefore has a **short absorption time**. Emery has seen patients improve on shortening time and *vice versa*,—but this is not invariable—L. i./11, 56. Further notes by V. B. Nesfield—L. i./11, 126

D'Este Emery in reply says practically all persons,—adults especially—have in their blood antibodies to the tubercle bacillus, therefore any diagnostic method must be quantitative, *e.g.*, the estimation of the time in which Complement absorption takes place with an Emulsion of Bacteria of definite strength under standard conditions.—L. i./11, 190.

Complement-Fixation reliable in diagnosis of an active or recently active tuberculosis lesion. Negative result also reliable.—A. Lisle Punch and A. Fleming, L. ii./20, 647; ii./24, 497. See also A. Sellers and E. N. Ramsbottom, B.M.J. i./21, 47. *Further refs. Edn. XVIII, p. 578.*

In a communication to the Medico-Chirurgical Society of Edinburgh, A. N. Smith and F. Hewat, stated the test might be of value in differentiating between an active and an inactive lesion. Sir Robert Philip considered test of no essential value so far as initial diagnosis was concerned, but thought it might

be in assessing the patient's condition from time to time. A. Rutherford, who had carried out 600 tests, considered the test of undoubted value in certain groups of cases, yielding a positive result when the clinical findings pointed otherwise, yet on later investigation correctness of the serum result was demonstrated.—B.M.J. i./24,15.

There are two opposite factors in the process of cure of an infective disease,—on the one hand an increase in the defensive forces tending to cause immunity, and on the other, a specific raising of the sensitiveness of the body to the microbe or its toxin so that it tends to become *less* immune. The latter process is called **Anaphylaxis** (opposed to prophylaxis). In the case of tuberculosis the first effect of a tuberculous lesion is to raise the susceptibility of all parts of the body to the tuberculous toxin. This substance—Tuberculin—is practically without action on a normal person. It is only when he is *sensitised* by a previous dose or doses that it becomes a real toxin. This process is in the highest degree disadvantageous to the patient,—the tuberculous fever when not due to secondary infection is apparently an entirely anaphylactic reaction to doses of Tuberculin too small to have any action on a healthy person. It appears, however, that this stage is essential to the production of immunity. Both anaphylaxis and immunity are specific—either may serve in diagnosis. The great *majority of adults have already acquired some immunity to tuberculosis*. Children very commonly have a small tuberculous focus (94% in Vienna amongst the poor become tuberculous before reaching the age of 14) causing no apparent symptoms. Everybody is being constantly vaccinated against the Tubercle Bacillus *via* the alimentary canal and lungs. The traditional peck of dirt must contain innumerable millions of tubercle bacilli. The immunisation or preventive treatment so caused is absent to a great extent in childhood. Adults as a class show sign of having been rendered partially immune to the tubercle bacillus and this renders the diagnosis by the immunity reaction more difficult than in children.—Von Pirquet's test is entirely satisfactory in childhood but of less value in adults.—W. D'Este Emery.—L. i./11, 485.

A. C. Inman on Complement Fixation Test.—L. i./14,1446.

Results of the test should carry some weight with the clinical observer and with a positive finding a very full investigation should be made before ruling out tuberculosis.—W. Broughton-Alcock and others.—L. i./25,1331.

Conference of International Union against Tuberculosis, London.—L. ii./21,301.

Annual Report of the Committee of the Privy Council for Medical Research, 1922-3, dealt with *defatting of tubercle and other bacilli*.

New methods for the study of the pathology and treatment of tuberculous disease.—Sir A. E. Wright, L. i./24,218.

Animal experiments show that residence in the animal body is often able to convert tubercle bacillus from simple saprophytes into highly virulent and pathogenic parasites.—B.M.J.E. i./24,12.

Rate of sedimentation of red blood corpuscles a test of remarkable accuracy in pulmonary tuberculosis. Generally speaking, the greater the rate of sedimentation the more severe and active is the disease. Very useful as a treatment.—B.M.J.E. i./24,4.

Typhoid Fever—Bacillus Typhosus.

Widal's Reaction (Serum Diagnosis).—Collect sample of blood in a small capillary pipette, and seal the ends, that nearest the blood being closed first. By pricking the lobe of the ear or the finger the blood will run into the tube by capillarity. The serum is allowed to separate, or the tube is centrifuged to cause as complete a separation as possible of corpuscles which may mask a reaction. The serum is blown out on to the corner of a slide and a platinum loopful is mixed with 9 loopfuls of normal saline solution, and one loopful of this 1 in 10 dilution is mixed with two loopfuls of typhoid broth, not more than 24 hours old, preferably filtered through ordinary filter paper. This 1 in 30 dilution is now examined as a hanging drop. Dilution of 1 in 50 and 1 in 100 should also be made. A control experiment must be conducted in addition.

Positive Reaction.—Complete: Clumping of organisms and cessation of movement as a rule in under 30 minutes, or may be instantaneous. Partial reaction: Sluggish movement providing the control is actively motile.

Negative reaction : No alteration in 1 hour. Dilutions 1 in 100 should give same results in 50 minutes ; if the time exceeds this the diagnosis is doubtful.

The reaction may also be performed in similar dilutions in sealed capillary pipettes (Wright). This constitutes the macroscopic method of applying Widal's Reaction.

Notes of Caution in Applying.—The broth itself or a control with normal serum should first be examined to see that the organisms are freely motile and show no pseudo clumps, as clumps are sometimes present in the broth before the addition of the blood. The serum of persons having previously had typhoid may react even years after. This may cause confusion where a typhoid diagnosis had not been given. Again, if only slightly diluted, e.g., 1 in 10, normal serum frequently 'clumps,' which is not the case on further dilution,—1 in 30 or 50 is safest. Some workers require a result with a 1 in 200 dilution within half an hour to be positive. Too great a dilution may obscure. The blood of *all* cases does not react, case may be too early (generally obtained about end of first week). Cases are recorded where reaction intermits, absent one day, present next, and again recurs, and also a few described where there was no reaction throughout the disease, but these are fortunately very rare.

A special culture should always be at hand—one known to react, as occasionally laboratory cultures do not respond.

Anomaly in the Reaction.—In examining blood of patients suspected of enteric group infections using Dreyer's Standard Method, 'Zone phenomena' were frequently seen, i.e. the occurrence of agglutination in higher dilutions of a serum while lower ranges failed to agglutinate. It is more striking by the macroscopic (Dreyer) method than the microscopic. It was found that the addition of another serum, non-agglutinating to the bacillus under test increases the zone of inhibition. The presence of salt in the test augments but does not cause the negative zone.—A. F. S. Sladden, L.ii./16,272.

Standard cultures and agglutinating sera for diagnosis by macroscopic agglutination tests are prepared at the Department of Pathology, Oxford, including *B. typhosus*, *B. paratyphosus* 'A' and *B. paratyphosus* 'B,' *B. dysenteriae* (Shiga, Flexner & Y.), *B. enteritidis* (Gaertner).—B.M.J.ii./16,595.

Even where typhoid is endemic, as in Syria, single agglutination tests are of value in diagnosis after the 8th day. The phenomenon of coagglutination requires further study. In investigation of the enteric group that agglutination tests should be made with as many organisms as possible.—E. H. R. Altounyan, L. i./24,75.

Macroscopic Agglutination.

The following is a convenient method much used in Germany : make dilutions of serum in ordinary test tubes, take a loopful of growth from an 18–24 old agar culture and emulsify in the dilution in the first tube, repeat in the second tube and so on. Make a control in normal salt solutions. Incubate and look for precipitates. A fine curdy flocculent ppt. indicates agglutination and a uniformly turbid emulsion a negative reaction.—Stitt.

The value and limitations of the agglutination tests in the diagnosis of the enteric group of organisms.—A. B. Rosher, L. ii./28,461.

Recognition of small quantities of *B. Typhosus* by complement fixation—in the mixed growth obtained on plates inoculated with an emulsion of fæces.—B.M.J. ii./10,1516.

Colloidal Silica. Has power to inhibit action of complement, and thus prevents lysis and destruction by bacteria of blood fluids. Experiments with fresh blood on typhoid bacillus.—W. H. Tytler, B.M.J. ii./22,980.

Characters of *B. Typhosus*.—*B. Typhosus* is a motile rod 4 μ long, but length varies on cultivation ; motility due to flagella, 12 to 16 in number. Gram—. Grows easily in ordinary media. Produces acid in glucose and mannite, sorbite in milk. No indol in peptone water.

Caffeine enrichment method for separating *B. Typhosus* from *B. Coli*, vide Bact. Water Examination. *B. Typhosus* is said not to grow in a medium containing 0.01% Arsenious Acid, whereas *B. Coli* will grow in a medium containing 1.5% of same.

Atropine Injection as a means of Diagnosis of the Typhoid group in affections. Atropine 1/33 grain hypodermically hardly increases the pulse rate in Typhoid and Paratyphoid 'A' and 'B' infections, whilst in normal

people and those suffering from other diseases it is accelerated. At least one hour should elapse after a meal. Give the injection and allow 25 minutes to elapse—patient remaining absolutely quiet before making second observation. As an arbitrary rule an increase of pulse rate by about 20 or more beats a minute after the injection may be accepted as an indication that patient is probably *not* suffering from typhoid or one of the paratyphoid series. If the increase is only 10 beats or less the reaction is suggestive of infection.—H. Fairley Marris, B.M.J. ii./16,717; ii./17,492.—The details of the method published as a report by the Med. Res. Com. L. ii/17,503.

Marris's Atropine Test of distinct and definite value in diagnosis of typhoid but of little value in paratyphoid group of fevers.—M. L. Treston, I.M.G. Oct., '26,479; also Dec., '26,588.

Petzetakis's Iodine Reaction a modification of, for diagnosis of typhoid fever. 25 Cc. of urine are saturated with 20 Gm. of crystallised Ammonium Sulphate. After 15 minutes, filter urine and dilute to one-third, if too thick. To 10 Cc. of filtrate add one-fifth its volume of a 10% solution of Sodium Hydrate and then a drop of 5% Tincture of Iodine. Shake solution, and if reaction is positive a persistent golden-yellow colour is produced. Reaction positive in the first week, increasing in intensity until disease reaches its height and then decreasing, becoming negative before temperature becomes normal. Also invariably positive in pulmonary tuberculosis with cavity formation, very frequently in second stage and occasionally in first stage. Often positive during height of pneumonia and measles, and always negative in malaria and acute rheumatism. Of greater diagnostic value than the diazo-reaction, owing to earlier appearance, greater constancy and longer duration.—L. i./24,245.

Russo's Test for suspected typhoid fever.

4 drops of a 0.1% aqueous Methylene Blue solution to be added to 4 or 5 Cc. of urine. Green coloration stated to be positive—blue, negative.

Flagella Stains.

MCCRORIE'S STAINS.—Solution A. Night Blue 1 in Alcohol, absolute 20, Alum 1 in water 20, Tannic Acid 1 in water 20. Mix and filter at once. Solution B. Aniline Fuchsin. To 100 Cc. of saturated Aniline Water, add 10 Cc. of absolute alcohol and 1 Gm. of Fuchsin, or Carbol-Fuchsin diluted may be employed.

VAN ERMENGEM'S STAINS.—A 1% Osmic Acid Solution, 100, Tannin 18, Water 45, B. Silver Nitrate Solution 0.25 to 0.5%. C. Gallic Acid 1, Tannin 0.6 Potassium Acetate fused 2, Water 70.

PITFIELD'S METHOD.—Solution A. Tannin 1 Gm. Water 10 Cc. Do not filter. Solution B. Saturated aqueous solution of Alum 10 Cc., saturated Alcoholic Gentian Violet Solution 1 Cc. Filter and keep in a stoppered bottle. Fuchsin will answer the same purpose as Gentian Violet. Equal parts A and B mixed, heated to nearly boiling and employed to stain 1 to 3 minutes, wash in water, dry and mount.

PLIMMER AND PAINE'S METHOD (For Flagella).—Rub down Tannin 10, Aluminium Chloride (Cryst.) 18, Zinc Chloride 10 and Rosaniline HCl. 1.5 with Alcohol 60% 10, then employ a further 30 of the Alcohol. In use the clean slide is baked and allowed to cool to blood heat and a drop of 18 hours culture placed at one end and allowed to run down by tilting. The film must dry quickly. One part of the stain is mixed with 4 parts water and after standing 60 seconds it is filtered on to the film and left on further 60 seconds, then washed rapidly. Finally stain with Carbol Fuchsin 5 minutes, wash and dry.

["**Crystal Violet**," and neutral red, advocated for distinguishing colonies of *B. Coli* (coloured red) from those of *B. Typhosus* (also *B. Enteritidis* Gartner and others), coloured blue to purple. Medium contains Sodium Taurocholate to inhibit growth of nearly all but intestinal bacteria. Lactose is another essential component of the medium as *B. Coli* and congeners decompose it with gas formation.—B.M.J. i./02,1473.

Conradi evolved a method of early diagnosis of typhoid fever. Researches demonstrated necessity of keeping the blood in a fluid condition, so as to avoid the disinfectant action of those substances which become active on coagulation. Bile is employed for this purpose; in addition, the medium contains 10% peptone and 10% glycerin. The blood from lobe of the ear is drawn into a

pipette containing a little bile and mixed with two or three Cc. of the Peptine-glycerin-bile medium in the proportion : blood 1, medium 3. Incubate at 37° C. for 10 to 16 hours and make cultures on agar plates according to the

Drigalski-Conradi formula *q.v.* Diagnosis can be effected by this method in 26 to 32 hours, and it is applicable as soon as the patient exhibits a febrile temperature.—B.M.J. i./o6,339.

Brilliant Green has been found of service in the elimination of *B. Coli* from cultures which have to be searched for *B. Typhosus*.—P.J.i./14,592.

With regard to persistence of this and other organisms in London water see Bact. Exam. of Water.

The bacillus could be recovered from bottles intentionally infected with it, in course of an investigation on best mode of disinfecting water for military use, even after washing out 12 times with sterile water.

Proteins of typhoid bacilli. Examination by Capt. S. R. Douglas and others under Med. Res. Council, B.M.J. i./22,74.

Typhoid fever outbreak in New York. Of 650 cases estimated due to an unusual etiologic factor, 506 (78%) gave a history of eating oysters.—Jl. A.M.A. ii./25,218.

B. Paratyphosus. *Paratyphoid* infection is dealt with in Vol. I. The disease is similar to typhoid, though generally running a milder course. Intestinal ulcers are identical with those of typhoid. Cases of mixed infection are not rare.—L. i./o7,284,1293,1571.

Distribution of certain bacilli of the food-poisoning group (*B. Suipestifer* and *B. Paratyphoid* ('B')) more limited in England than abroad.—B.M.J. ii./10,1503.

Paratyphoid infection may resemble meat poisoning.—F. A. Bainbridge, L. i./12,705, 771, 849.

Cole & Onslow's Tryptic Broth. A broth using Casein (Lait-proto No 6, for bacteriological purposes), digesting this with fresh Pancreatic Extract and adjusting the reaction by making the Hydrogen-ion concentration about pH = 7.35.

This reaction is very near that of blood serum and also near the optimum for the growth of most pathogenic organisms.

The broth gives luxuriant growth with the colon-typhoid group, also with *B. diphtheriæ* and the *meningococcus*. It is most useful for testing for *Indol* formation owing to its rich content of free tryptophane. When diluted with its own volume of 0.5% Sodium Chloride it is an excellent medium for detection of *acid and gas* formation. It is also good for making Agar media.

Phenolsulphonaphthalein is employed in the medium to differentiate *B. typhosus* and *B. paratyphosus* 'A' and 'B' by a method based on the H ion concentration reached in growth of the organisms. For the separation of 'T' from 'A,' formation of gas in glucose and the rapid fermentation of dulcitate by 'A' and not by 'T' are relied on.

Phenolsulphonaphthalein is useful as indicator. Does not appear to inhibit growth and is more sensitive than litmus. Lemon yellow in acid solution and red or magenta in alkaline. Solution of strength 0.04% is added to the **Glucose Tryptic Broth** and a **Dulcitate Medium** in proportion of 4% of the solution.

Following are the critical points of difference:—

Organism.	Solution "G." Glucose Tryptic Broth and Phenolsulph- onaphthalein.	Solution "D," Dulcitate Tryptic Broth and Phenolsulph- onaphthalein.	Glucose ferment- ation tubes.
<i>B. Typhosus.</i>	Yellow.	Red or pink.	Acid.
<i>B. paratyphosus</i> "A."	Yellow.	Yellow.	Acid and Gas.
<i>B. paratyphosus</i> "B."	Red or pink.	Variable.	Acid and Gas.

Paratyphoid B. Group. Differentiation of *Aertryke B.* from, also subdivision of the *Aertryke* organisms.—H. Schütze, L. i./20,93.

Paratyphoid 'C' bacillus as a cause of paratyphoid fever.—L. S. Dudgeon and A. L. Urquhart, L. ii./20,15.

Importance of protection against paratyphoid as well as against typhoid is dealt with fully in Vol. I. Details of procedure for Agglutination Test.—Prof. Dreyer, E. W. A. Walker and A. G. Gibson, L. i./15,324.

As **paratyphoid A is almost unknown** in this country and typhoid is not a serious risk, it would be sufficient in a para-B outbreak to give a pure *paratyphosus B* vaccine. The number of organisms can thus be greatly diminished and the reaction lessened. *To give the full anti-typhoid-paratyphoid vaccine for fear of a paratyphoid epidemic is like ensuring against accidents by all means of transport when about to travel by aeroplane!* Large doses of T.A.B. are not likely to make inoculation popular and are seldom necessary.—L. ii./28,454.

Living autogenous Vaccine used.—B.M.J. i./15,584.

Fermentation Reactions of B. Typhosus.

W. J. Penfold, dealing with fermentation of Lactose, Peptone Water and of **Dulcite*** Water by *B. Typhosus*, states it does not ferment arabinose. Fermentation of glycerin and papillæ formation on Isodulcite.—B.M.J. ii./10,1672. Raffinose, erythritol and adonite are not fermented.

The fermentation of Lactose—or non-fermentation—provides vastly important information as to the coli-typhoid organisms.

The non-Lactose fermenters include the organisms of typhoid and paratyphoid, bacillary dysentery and acute bacillary enteritis, whilst fermenters include *B. Coli* and its numerous subtypes, all of which are of minor importance by comparison with the highly pathogenic species met with among the non-Lactose fermenters. There are, however, non-Lactose fermenters—saprophytes—of no greater importance than *B. Coli*. For a paper on faecal flora of whites and natives in Uganda, see H. H. Duke, L. ii./21,1212,1288.

The sodium salts of *d*-Tartaric, *l*-Tartaric, *meso*-Tartaric, Citric, Fumaric, and Mucic Acids for differentiating bacteria where sugar reactions fail.—B.M.J. ii./26,565.

Biochemical characters of certain bacteria when living in association or artificially mixed, *e.g.*, the mixture of two species *B. typhosus* and *B. morgani* may produce gas in some instances, though one species produces only simple acidity, never gas, and the other neither acidity nor gas.—A. Castellani, B.M.J. ii./25,735.

Typhoid Carriers. On a basis of three persons liable to excrete Typhoid Bacilli per 1000 of population London alone would contain more than 14,000 carriers. The total number of known enteric fever cases in London in 1908 was only 1,357. Carriers however numerous have not prevented the conspicuous decline which has taken place in the prevalence of enteric during the last half century—hence the danger of the average carrier would appear negligible,—measures at present employed in the prevention of the disease seem adequate to cope with the 'carrier' also.—L. ii./10,1631.

Bacteriology of human bile with especial reference to the typhoid carrier problem. Of 100 Cases 23 were sterile, in 51—or a half—*B. Coli* was isolated in pure culture. *B. Coli* is more frequently found when death is due to intra-abdominal disease than when it is due to affection of other parts. It was, for example, isolated in every case except one, in which death was attributed to appendicitis or peritonitis, but was not once found when it was due to cardiac disease. In only four cases were bacilli of the typhoid-paratyphoid group isolated. There are at large individuals never supposed to have had typhoid fever who are in reality chronic typhoid carriers.—Q Jl. Med. Jan. 1911.

Brilliant Green and Telluric Acid Isolation Method for Typhoid and Paratyphoid Bacilli. Make the usual smear cultures on plates of Endo's or MacConkey's medium. Simultaneously inoculate peptone water containing Brilliant Green. Employ in preference a series of tubes for each specimen, but when time prevents this use a concentration of 0.5 Cc. of 1 in 10,000 Brilliant

*Dulcitol is synonymous with Dulcite and Melampyrite $C_6H_8(OH)_6$, a sugar from *Melampyrum nemorosum* and other *M.* and *Euonymus* species. It occurs in white crystals soluble in water, slightly in alcohol.

Green in 10 Cc. of medium. Incubate both and if typical colonies are not present or scanty in the solid medium make sub-cultures from the Green tubes into the above mentioned solid media. Incubate.

Telluric Acid is also advised 0.4 Cc. of 1 in 1000 solution with varying amounts of Brilliant Green per 10 Cc. of medium. *B. Typhosus* can sometimes be recovered from fæces by this combination better than in Brilliant Green alone.—C. H. Browning & L. H. D. Thornton, B.M.J. ii./15,248. See also Jl. Path. & Bact., XIX., 1914, p. 127, in which Potassium Tellurate is similarly advised.

The method is useful for detecting a number of carriers. **Brilliant Green has a specially inhibitory effect** on the colon bacillus as contrasted with typhoid and paratyphoid bacilli, whilst it has a powerfully bactericidal action on practically all other organisms. Telluric acid is included in the media because it was found that certain organisms giving the ordinary reactions of the enteric group but differing from them in fermenting inositol escaped the action of the Brilliant Green alone but were killed off by the addition of Telluric Acid. Browning's work supported.—A. Leitch, B.M.J. ii./16,317.

Phenol and Brom-Cresol Purple as indicators in the bacteriological examination of stools. May be used in the preparation of Lactose-agar plates for the isolation of members of the typhoid-dysentery group. Employed successfully with brilliant green in isolation of typhoid-paratyphoid group.—A. M. Chesney, per Jl. Trop. Med., April 15/22,105.

Endo's Medium.—Beef Extract 5 Gm., Peptone 10 Gm., Agar 30 Gm., Dist. Water to 1,000. Dissolve on water bath, adjust to neutral reaction to Phenolphthalein, filter and sterilise. To make plates prepare 10% Anhyd. Sod. Sulphite Solution and to 10 Cc. of this add 2 Cc. Fuchsin Solution (Basic Fuchsin 10 Gm., Alcohol 100 Cc.) and steam 5 minutes in water bath. To each 100 Cc. of the Agar mixture add 1 Gm. Lactose, dissolve in water bath and add $\frac{1}{2}$ Cc. Fuchsin-sulphite Soln.—U.S.D.

By placing a circle of blotting paper in the lids of the Petri dishes before sterilising them, all the water of condensation is absorbed; this aids greatly in making successful cultures.

The use of the medium with agglutination test is expeditious in isolating *B. Coli* and the para-typhoid organisms. *B. Coli* (being acid-forming) are golden-metallic looking. *Streptococci* form crimson dots. Suspicious colonies (grey coloured) are plated on to Hiss Medium.

Hiss Medium.—Dissolve Lemco 5, Sodium Chloride 5, in distilled water 1000 in the autoclave at 120° C. for 5 minutes. Add washed Agar 8 Gm. and melt in autoclave at 130° C. for 5 minutes. Add washed Gelatin 80 Gm. Dissolve and cool to 45° C. Clear with white of one egg at 120° C. for 5 minutes, filter and add 1% Dextrose and sterilise in steamer 1 hour. Fill 5 Cc. tubes and sterilise in steamer again. This medium remains solid at 37° C.—F. B. Bowman.—B.M.J. ii./17,250.

Flies as Typhoid Carriers.—Investigations show that bacilli injected into the flies' intestines can be recovered as long as six days afterwards. The bacilli were found in the flies' fæces during the space of two days. Similar results with Gaertner's B. but the bacilli were not recovered from the fæces.—B.M.J. ii./10,1271.

Flies in relation to typhoid fever, dysentery, etc. Prof. C. J. Martin concludes:—The facts brought forward in the statistical paper do not necessitate recourse to the hypothesis that carriage by flies dominates the situation. The fly hypothesis is the only one offering a satisfactory interpretation of the extraordinary dependence of the epidemic upon the accumulated effect of temperature. It offers further a ready explanation of the spread of infection to neighbouring children who have no direct personal contact with the patient. Peculiarities of the relation in times between fly prevalence and the epidemic in different localities are not inconsistent with the view that fly carriage is essential to epidemicity. No other interpretation so far forthcoming is nearly so satisfactory.—B.M.J. i./13,1; L. i./13,1.

Cattle and horses as typhoid carriers may explain the erratic behaviour of this disease.—L. ii./12,1543.

B. Typhosus is very **susceptible to acidity**. In wine it rapidly disappears while wine added to water will reduce number if present. 20 Gm. of vinegar per litre kills *B. Typhosus* in an hour. Vegetables eaten raw

ould be treated with water acidulated with 10 Gm. per litre and left in
ame for about 1½ hours.—L. i./15,511.

B. Aertrycke infection—three cases. Distinction between this organism
and *B. paratyphosus* 'B.'—B.M.J. ii./18,310.

Study of 63 strains belonging to paratyphosus B group; all produce acid
and gas in Arabinose, Dulcitol and Xylose, and all but 5 produce transient
acidity in Inositol; all ferment Trehalose and blacken Lead Acetate medium,
differentiating them from organisms of *enteritidis* and *suipestifer* groups.
Capable of division into two sharply-cut groups; 33 strains, containing all
strains isolated from paratyphoid fever in man, and nearly all *paratyphosus* B.
strains of porcine origin—suggested name for this group, "Schottmüller
type"; the other group of 27 strains all isolated from food-poisoning out-
breaks, together with all strains of rodent origin—as all in this group agree in
ability to absorb homologous agglutinins from *aertrycke* "mutton" serum,
the suggested name is "*Aertrycke* Type." Both groups more closely allied
to each other than to *B. enteritidis* type.—B.M.J.E. i./24,44.

A case of "parenteric fever" probably due to *B. Columbensis Castellani*.
—L. i./25,381.

Outbreak of milk poisoning in Aberdeen affecting 300 persons—acute
diarrhoea and vomiting, but no deaths—traced to milk containing organisms
of typhoid-dysentery group, apparently derived from a byre or farm worker.
—B.M.J. ii./25,229.

Paratyphoid outbreak traced to ice-cream.—L. ii./25,823.

A typhoid-carrier survey of 1,076 healthy dairy employees in Alabama
yielded 55 carriers of typhoid and paratyphoid bacilli, i.e., 5.1%. —S.W.
Welch and Co-workers, JI. A.M.A. ii./25,1038.

Typhus Fever.

Treatment.—Support the heart by Digitalis or Strophanthus, large
injections of Camphorated Oil, injections of Rhus, and injections of Adrenalin
if syncopal attacks occur. Avoid antipyretic drugs. Optoquin 1 to 2.5 Gm.
daily *per os* has been advised by German physicians to be taken so long as
patient can swallow. When coma supervenes, to be given in oil hypoder-
mically. Said to cut short the fever and lessen mortality.—B.M.J. i./16,621.

Notes on about 1,800 cases in the Serbia epidemic 1915. Incubation
period varies from 5 to 14 days. Usually a period of 12 days—onset of 2 days
and a fever of 16 days resolving in lysis. Careful nursing essential. Washing
the mouth out with **Permanganate** or in preference **Hydrogen Peroxide**
obviated parotitis, otitis and the like. Alcohol thought to aggravate cerebral
symptoms. Ice to the head.—T. Gwynne Maitland, B.M.J. ii./15,283.

Nose breathing valuable precaution.—B.M.J. ii./15,492.

2,000 cases in a German prison camp. Patients did well on the starvation
diet. Camphorated Oil hypodermically, but not found good; much abscess
formation. **Morphine** is a sheet anchor. Expectant and symptomatic
treatment best.—P. C. T. Davy and A. J. Brown, B.M.J. ii./15,737.

Tabardillo is typhus as it occurs endemically in Mexico.

A person unprotected by a previous attack exposing himself to a typhus
patient in a close room runs risk, though there are no lice present. **Ventila-**
tion essential.—J. W. Allan, B.M.J. ii./15,841.

There is high fatality among the prosperous classes.—B.M.J. i./16,705.

Chadwick Lectures on Typhus in Serbia—a full description—flourishes in
war time owing to overcrowding, etc. **Kerosene** or equal parts of Kerosene
and soft paraffin for anointing the body is an efficient insecticide.—R. O.
Moon, L. i./16,1069,1111,1157.

Antitoxin encouraging (Nicholle and Blaizot from the Pasteur Inst. Tunis.)
start early. Daily hypodermic doses of 10 to 20 Cc.—L. ii./16,950.

Prophylactic inoculation. A serum made by passage of the virus through
the monkey is preventive.—S. Kusama, L. ii./21,386.

Rickettsia bodies isolated from blood of typhus patients—suggested as agent
of typhus.—Lieut.-Col. Froilano de Mello, JI. Trop. Med., Jan. 15/23,24.

Typhus fever epidemic among the Greek refugees—treatment described.
Rum treatment not adopted.—Sir P. Hehir, L. ii./23,153,209,264.

S. African typhus, 8,000 cases a year among natives. It is a comparatively
old type; the infected louse the cause. Hot air deverminisation apparatus
working for 20 minutes at 75°C. advised. Naphthalene 1, in Nut Oil 8, is an
efficient insecticide (curiously, it has no smell) for disinfecting head and body,

while clothes are going through the machine; it kills lice and nits on hair and body. It has beneficial effect on scabies.—H. F. Sheldon, L. ii./23,1075.

OLDER REFERENCES. See *Edn. XVIII.*, Vol. II., p. 584.

Weil-Felix Reaction is distinctive. The X2 and X19 strains of *proteus* are agglutinated by the serum of typhus cases. It is similar to the Widal reaction.—Jl. R.A.M.C., July 20/23,210.

The reaction must be interpreted with caution. Conclusive in very high titres, above 1:1000; titres of 1:100 very suggestive, but 1:50 only indicate possibility of typhus. Unusual for reaction to be so pronounced in diseases other than typhus as to be regarded as positive, but it is occasionally positive in scarlet-fever and small-pox, and most likely to be so in Paratyphoid fever—a case in point. Rise of titre during disease a strong argument in favour of typhus. Author recommends examination by both Weil-Felix and Widal Tests, also, in sporadic cases, by Nicolle's method (injection of 0.25 Cc. of serum into peritoneum of guinea-pig or monkey.) In positive cases, after incubation period of 10 days, fever sets in lasting 6-12 days. Negative result has significance.—B.M.J.E. i./24,36.

The strength of the reaction does not correspond to the gravity of the disease. Mild cases may give strong reactions, but a high reading was also obtained in a patient shortly before death.—E. H. R. Altounyan, L. i./24,76.

Bacillus Vaginæ, Doederlein's.—

An aerobic organism, Gram+ (often feebly), constantly found in the normal vaginal secretion in adults. Facultative anaerobe. non-motile. non-pathogenic. The only definite organism of the vagina. Plays the important role of preventing development of other bacteria, especially pathogenic production of Lactic Acid.

In a series of examinations of the vaginal secretion in infants the organism was absent. In more than half the cases (ranging from 30 minutes old to 3 days) the fluid was sterile. The reaction of the secretion is (normally) acid in the majority of cases,—not due to action of micro-organisms. Amongst the organisms found were a yellow *Staphylococcus liquefying gelatin* and white *Staphylococci* not liquefying.—P.R.S.M. Obst. Sect. Nov. 10, 26.

Weil's Disease.—The term would be desirably abolished. For cases of the kind in which no specific spirochete or other infection are found it would be better to use the term **hæmorrhagic infective jaundice**. A form of hæmorrhagic infective jaundice has been called variously Mediterranean yellow fever, Weil's disease, spirochætosis icterohæmorrhagica, etc., which is unscientific.—Sir W. H. Willcox, B.M.J. i./19,707.

Leptospira icterohæmorrhagiæ appeared in 1916 in Flanders as the cause of a form of febrile jaundice.—A. Stokes and J. A. Ryle.—B.M.J. ii./16,41. E. W. Andrewes, i./17,830; Lord Bertrand Dawson, ii./17,345; see also Sir W. Herrington, i./19,20.

The spirochete causes epidemics in Japan.—B.M.J. i./16,627.

London occurrence of Weil's disease. A seaman who fell overboard and swallowed a lot of Thames water at Gravesend, became exceedingly ill (almost complete deafness during initial fever) and his blood on injection into a guinea-pig caused typical phenomena of Weil's disease. Neokharsivan 0.15 Gm. was given with little or no effect. No history of contact with infected rats. Water infection is known to be possible by past experience.—P. Manson-Ball and co-workers, L. ii./22,1056.

L. icterohæmorrhagiæ discovered in wild rats caught in slaughter houses in Warsaw—4 out of 42 infected. Two strains possessed very high virulence for guinea pigs. From experiments the isolated leptospira concluded to be identical with *L. icterohæmorrhagiæ*.—Ludwig Anigstein, Jl. Trop. Med. Mar. 1/23,81.

Spirochaetal jaundice. Report of small epidemic in Edinburgh.—i./25,504.

L. icterohæmorrhagiæ present in London tap water, and may cause outbreak of spirochaetal jaundice, especially in abnormal circumstances.—Hindle, B.M.J. ii./25,57. See also p. 442.

Investigations on jaundice of bacterial origin.—L. Anigstein and Z. Milinski. Jl. Trop. Med., Nov. 15/23,337. Review of data.—B.M.J. i./21,206.

A case of Weil's disease contracted by the 'whip' of a pack of foxhounds.

Following p.m. of puppies which had died from 'yellows' (a leptospiral disease of dogs). The association of human with canine jaundice may not be so uncommon as the recorded cases suggest. The virus is easily transmissible by skin contact.—C. J. M. Lawrence and C. C. Okell, L.ii./29,328.

VAN DEN BERGH REACTION (EHRlich's DIAZO REACTION APPLIED TO BLOOD SERUM CONTAINING BILIRUBIN) *for obstructive or impaired liver function.*

The reagent consists of : *Solution I.*—Sulphanilic Acid 1, Hydrochloric Acid P. 15, Water to 1000. *Solution II.*—Sodium Nitrite 0.5, Water 100. For use, 25 Cc. Solution I. are mixed with 0.75 Cc. Solution II. and this mixture must be freshly prepared for each test.

Direct Test (Qualitative). Add 1 Cc. of the reagent to an equal volume of serum diluted with 2 Cc. distilled water. A bluish-violet colour beginning immediately and becoming maximal in 10—30 seconds is called an immediate direct action, indicating presence of uncombined bilirubin and the existence of mechanical obstructive jaundice, as in cholangitis. A reddish coloration beginning after 1 to 15 minutes and deepening to violet is called a delayed direct reaction, indicating impaired liver function, as in acute yellow atrophy. A reddish colour appearing at once and deepening to violet is called a biphasic direct reaction, indicating both obstructive jaundice and impaired liver function.

Indirect Test (Qualitative).—To 0.5 Cc. serum add 1 Cc. 95% Alcohol and centrifuge. To 1 Cc. of the supernatant fluid add 1 Cc. reagent. If positive violet colour appears at once and points to hemolytic jaundice.—Jl. A.M.A. /28,1395.

Indirect Test (Quantitative).—To 1 Cc. serum in a 15 Cc. graduated tube add 0.5 Cc. reagent. After a minute or two add 2.5 Cc. 95% Alcohol and 1 Cc. saturated Ammonium Sulphate solution. Mix well and centrifuge. Read the quantity of supernatant fluid and the dilution of the bilirubin (approx. 1 in 3) contained in the serum is directly obtained (dilution of unknown). The alcohol solution (the unknown) is then compared with a standard solution and the amount of bilirubin computed as follows :

$$\frac{\text{Standard}}{\text{Unknown}} \times \text{Dilution of unknown} \times 5 = \text{mgr. of bilirubin per litre of serum.}$$

The Standard is made as follows : *Solution 1.*—Ammonium Ferric Alum 1508 Gm., Conc. Hydrochloric Acid 50 Cc., Distilled Water to 250 Cc. (keeps definitely). *Solution 2.*—Of Solution No. 1, 10 Cc., Conc. Hydrochloric Acid 25 Cc., Distilled Water to 250 Cc. (keeps a month). The *Standard which is freshly made* consists of Solution No. 2, 3 Cc. Ammonium Thiocyanate 10% and 3 Cc. Potassium Thiocyanate 20%, Ether 12 Cc.

Shake Standard thoroughly. The Ether extracts the colour from the solution and forms a supernatant layer which may be used in colorimetric comparison. The Standard matches in colour a dilution of 5 mgr. of bilirubin per litre of serum. The normal amount of bilirubin is from 1 to 3 mgr. per litre. Clinical jaundice is present with about 18 mgr.

Standard for Van Den Bergh's Test.

The colour given by 0.7 Cc. N/10 Potassium Permanganate solution diluted to 50 Cc. with water is equivalent to 5 in 10⁶ of bilirubin.—B.C.A., Sept. '28, 048.

References.

The Test is less satisfactory than at first hoped. Very variable results obtained in toxic cases. In genuine obstructive cases, immediate direct action was obtained, and in hæmolytic cases an indirect reaction. In doubtful cases the test failed.—B.M.J. i./24,279; see also *ibid.* 496, and L.i./27,384.

The Test for "latent" jaundice, during treatment with Arsenobenzol, has been found of greater value than either the Lævulose Tolerance Test, the Tense Test or the "Hæmoclastic Crisis" Test, and is a great advance towards the scientific control in the use of this dangerous drug. As soon as a condition of "latent" jaundice was detected Arsenical treatment was at once stopped and Glucose given freely. The small amount of serum necessary for the test is readily obtained when taking blood for Wassermann reactions.—I. Gerrard, B.M.J. ii./24,225

Van den Bergh Reaction. Improvement in technique. Of value.—J. N. McKee and C. H. Keefer, B.M.J. i./22, 716, 783; ii./25, 52. Of questionable value for differentiating between obstructive and non-obstructive types of jaundice in infants and young children.—Am. Jl. Dis. Child., per Jl. A.M.A. ii./25, 927. Normally, the Bilirubin content is between 0.2 mgr. to 1.0 mgr. per 100 Cc. of serum.—Klin. Woch., Aug. 27, '25, per Jl. A.M.A. ii./25, 117. Of use, even in the absence of clinical manifestations. Thanhauser and Anderson's Modification the most dependable for quantitative estimation.—per Jl. A.M.A. ii./25, 1337. Utility doubted.—D. Davies, L. i./27, 384. Applications of Van den Bergh's Test in surgery.—E. R. Flint, L. ii./27, 165; Y.B.P. '27, 65-6. *Meulengracht Test* for jaundice.—Jl. A.M.A. ii./25, 765. *Fouché Test* for hyperbilirubinemia, Jl. A.M.A. ii./25, 766 (for full description of test see Comptes Rend., 80: 826, 1917). An increase of blood bilirubin found in 35% of pregnant women and in 71% of women during childbirth: especially high in eclampsia.—per Jl. A.M.A. ii./25, 861. See also Press. Med., 1922, 29, 441, J.A.M.A., 1922, 77, 235, Y.B.P., 1922, 33, P.J. i./24, 584.

Further Liver Function Tests are Bromsulphalein and Phenoltetrachlorophthalein, q.v.

Whooping Cough.—**Bordet's Bacillus.**—A cocco-bacillus, non-motile, Gram-negative, staining feebly, regarded as causative of whooping cough, has been isolated. Cultures of the organism were found to be specifically agglutinated by the serum of children suffering from. Agglutinating reaction not strong. See also Vol. I., p. 956 and Therapeutic Index.

Resembles *B. influenzae* (Pfeiffer) somewhat and grows somewhat scantily on blood agar. The following medium permits of isolation from sputum: Potato 500 Gm., 4% Glycerin solution 1000 Cc. Autoclave and pour off excess fluid. Emulsify potato in Normal Saline 1500 Cc. and add Agar 3 to 4%. For use mix with equal quantity of defibrinated blood.

Pertussis shows a mononuclear leucocytosis of 15,000 to 50,000.—Stitt.

Out of 1,115 cases of whooping cough 29% showed *B. pertussis*, and out of 533 proved cases 41% showed the organism, which in three cases was isolated 24 hours before the whoop commenced. Suggested that the quarantine period should include the catarrhal stage: thus 30 days from onset of catarrhal symptoms would include 94% of all possible spreaders, as against 62% under present American regulations.—B.M.J.E. ii./27, 72.

Frequency of finding Bordet's Bacillus diminishes markedly after end of the 4th week of the spasmodic phase.—B.M.J. ii./26, 663.

The bacillus isolated in cases examined within the first week. A peak-like colony developed after 3 days' incubation. Easier and more exact than bacterial diagnosis of diphtheria.—H. Sugare and J. W. McLeod, L. ii./26, 167.

Yaws. *Syn. Frambæsia.* A contagious inoculable disease characterized by an indefinite incubation period followed usually by fever, by rheumatic pains, and by the appearance of papules which generally develop into fungating, encrusted, granulomatous eruption.

An organism found in the lesions of yaws has been named both *Spirochaeta pallidula* and *Treponema pertenue*.—Manson.

FRAMBÆSIA in Ceylon. Potassium Iodide in large doses best routine treatment; Atoxyl, Sodium Cacodylate, and Quinine Cacodylate also useful.

Novarsenobenzol has a rapid and remarkable curative action in every stage of the disease.—Manson.

Yellow Fever.

Yellow Fever resembles Weil's disease but the symptoms are more severe and hæmorrhages into the stomach and intestine cause black vomit and melæna. Has a very high mortality rate.

The Americans, Reed, Carroll, Agramonte and Lazear established that Yellow Fever is transmitted by *Aedes ægypti* *Syn. Stegomyia calopus*, *S. fasciata*. The virus can be transported from one place to another. For its development it requires a temperature of over 75° F. It ceases to spread below 75°. Usually it is a sea coast disease. The germ cannot be cultivated on ordinary lines and it is not a visible bacterium. It is a filter passer. The mosquito is the intermediary but it is not transferable by recently infected mosquitoes. The parallelism between the etiology of yellow fever and malaria is very complete. The germ is probably of protozoal nature. One attack generates

confers permanent immunity.—Manson. Noguchi thought the disease is due to *Leptospira icteroides*, but it is probably caused by a virus which will pass the pores of Y and N Berkfeld filters but not through W.—B.M.J. i./28,723.

L. icteroides will grow in a medium consisting of serum 1 part, Ringer's solution 3 parts, made semi-solid with 0.3% Agar and contained in tall tubes at the bottom of which is placed 1 Cc. of citrated yellow fever blood. A thin layer of Liquid Paraffin is poured on the top of the medium. *L. icteroides* is said to be $4.9 \mu \times 0.2 \mu$ wide. Grows best at 33°C . (91°F).—Stitt (1927). For a descriptive account see A. E. Shipley, B.M.J. i./15,921.

Serum of convalescent patients and animals promising.—B.M.J. ii./19,48. Noguchi's Researches, *ibid.* 283.

Yellow fever contracted by non-immune persons in spite of vaccination. Infection occurred while protection was developing. Possibility of immediate protection by anti-icteroides serum—0.2 Cc. sufficient to protect guinea-pigs for 10 days. For a man weighing 80 kilos, 15 Cc. should be sufficient to secure immunity for same period, *i.e.* until vaccination attains its final effect.—Hideyo Noguchi per Jl. Trop. Med. Jan 1/23,13.

Observations on prophylaxis.—A. Agramonte, Jl. Trop. Med., Nov. 1/24,285.

Yellow fever no longer exists in North America, Central America is almost free and Brazil "has reached the final bout with the disease."—L. ii./24,385.

Experimental studies in Northern Brazil.—H. Noguchi and Co-workers, Int. Conf. Trop. Am., '24,169-179.

Histopathology and hæmotology.—H. R. Muller, *ibid.*, 180-193. In the epidemic in Belize (1921), 17 cases were treated with Noguchi serum. Of 13 receiving serum on 1st or 2nd day only one died, but the remaining 4, who did not receive serum until 4th or 6th day, all died. Treatment only of value in midst of an actual outbreak—anti-mosquito work should be continued.—J. Cran, *ibid.* 194-200.

Prophylactic vaccine and curative serum of doubtful value and liable to give a sense of false security, causing relaxation of sanitary measures. Specificity of *L. icteroides* still remains to be proved. Serologic differences between it and *L. icterohæmorrhagicæ* are not pronounced, yet the fever and Weil's disease are clinically and pathologically entirely unlike. *L. icteroides* possibly a symbiotic organism in yellow fever, possibly the one inducing the hæmorrhagic phase. The symptoms, lesions and conditions which *L. icteroides* cause in animals are practically identical with those caused by *L. icterohæmorrhagicæ*, the etiologic factor in Weil's disease—Int. Conf. Trop. Am., '24,201-208.

As Noguchi admitted that the organism isolated by him and named *L. icteroides* is indistinguishable from that described by Stimson (1907), *L. icterohæmorrhagicæ*, the latter would appear to be the correct name.—Wenyon.

Prophylactic serum not intended to supplant anti-*Stegomyia* campaigns. Yellow fever and infectious jaundice both caused by a filtrable organism, both non-contagious, and both characterised by jaundice, hæmorrhage, acute hepatitis and nephritis, and relative brachycardia. In both, an attack confers lasting immunity. The clinical symptoms are very similar. *L. icteroides* is slightly thinner and shorter than *L. icterohæmorrhagicæ*. Serologically, the former gives a positive Pfeiffer reaction with serum of yellow fever convalescents, while the latter does not. Vaccine appears to give protection to non-immunes for about 5 or 6 months. Statistics given.—H. Noguchi, Int. Conf. Trop. Am., '24,209-220.

(Noguchi died in 1928 in a fever-stricken seaport of the Gold Coast, a victim of African yellow fever, of which he had just identified the cause, as a result of studying *his own case*.)

Of 7 cases treated with serum all recovered except one. Amongst 748 non-immune persons vaccinated with the killed cultures of *L. icteroides* 2 cases occurred, as against 199 cases amongst unvaccinated in Vera Cruz.—T. J. LeBlanc, Jl. Trop. Med., May 1, '25,178.

Methods of examination of *Leptospira*; new method for examining living pirochetes.—A. C. Coles, Jl. Trop. Med., June 15, '26,170-172.

Encouraging prophylaxis obtained with a Phenol-Glycerin Vaccine prepared from the liver and spleen of infected monkeys. Further work in progress.—E. Hindle, B.M.J. i./28,977.

OLDER REFERENCES:—

Yellow Fever is endemic amongst natives of the West Coast of Africa: it has been repeatedly mistaken for other diseases (often called "bilious remittent fever") or entirely overlooked.—B.M.J. i./11,249,301,491. Yellow fever

in Yucatan (Mexico). The natives are assumed to be immune from childhood.—L. ii./12,1812,1830. Further data 18th Edn., Vol. II.

A resume of researches on, *vide* L. i./14,1408.

Dengue.—Dengue resembles sand-fly fever but the febrile period is longer and relapse is more common. Sand-fly fever occurs in all the countries round the Mediterranean and extends into India : dengue occurs typically in Australia but is recorded from India, Africa, and other places. It would seem probable that the causative organism of sand-fly fever is the *leptospira* of Weil's disease. Rheumatic-like pains in the febrile stages.

The insect vector of dengue, in Manila and probably elsewhere, is *Aedes aegypti* (*S. fasciata*, as it used to be called), confirming the work of Cleland, Bradley and McDonald in Australia; it is not *Culex quinquefasciatus* (*C. fatigans* of old).—B.M.J. ii./26,489.

Points of similarity between Y. Fever and Dengue.—B.M.J. ii./17,105.

The differential diagnosis of dengue and influenza.—E. P. Thurston, *per* Jl. Trop. Med., Nov. 15/23,344.

Recent epidemics of dengue.—B.M.J. ii./28,806.

Transmission and etiology.—I.M.G., Aug. '25,377; *see also* A. C. Chandler *ibid.*, Oct. '25,460.

An undesirable degree of complication has been imparted to the subject. Claims to the discovery of "new" diseases would in most cases be recognised as unjustified if the authors were aware of the following facts in connection with the fevers of the dengue group. (1) Fevers of the dengue sand-fly group may last from 1 to 7 days. (2) They show a great variety of symptoms—in fact, the only common clinical features are the sudden onset and short duration. (3) They are extremely common and widespread over the tropics and sub-tropical world. (4) They may occur as sporadic cases in an endemic area, or as intense epidemics.

If dengue is regarded as a disease in which break-bone pains, a two-phase fever and a secondary rash are essential features, it is not surprising that medical men should look upon outbreaks of fever in which these characteristics are absent as distinct diseases.—J. W. D. Megaw, *per* Jl. Trop. Med., Nov. 15/23,347.

STAINING METHODS.

Gram's method of differentiating Organisms in Film Preparations :—

1. Treat with Aniline-Gentian-Violet 3—5 mins. 2 Without washing, add Gram's solution $\frac{1}{2}$ to 1 min. 3. Pour off Gram's solution. wash in water, rinse with alcohol three times, each of 10 seconds duration. Counterstain with neutral red 0.5% or weak Carbol-Fuchsin $\frac{1}{2}$ minute. 4. Wash in water. Dry.

Gram's Iodine solution has the formula :—Iodine, 1 Gm ; Potassium Iodide, 2 Gm. ; Water, 300 Cc.

NOTE.—Aniline-Gentian-Violet is prepared by adding 1 part of concentrated alcoholic solution of the dye to 9 parts of a filtered saturated solution of anilin oil in water (solubility about 1 in 30). P.G.V. directs 7 Cc. of the Saturated Alcoholic Solution of Gentian Violet with a further 10 Cc. of Absolute Alcohol to be added to 100 Cc. of filtered Aniline-Water. This may overcome 'muddiness.'

Gram-Eosin Method for Sections.—1. Place a little alcohol on section $\frac{1}{2}$ min. 2. Cover with filtered Aniline-Gentian-Violet 10 mins. 3 Gram's solution, 3 mins. 4. Decolourise in Alcohol. Wash in water. 5. Stain with Eosin 1—2 mins. Wash in water. 6. Dehydrate with Alcohol. 7. Clear with Xylol, mount in Xylol Balsam.

Eosin - Gram - Weigert - method. — Eosin (5% aqueous) 5 to 10 mins. Wash in water. Aniline-Gentian-Violet 10 minutes without washing. Gram's iodine solution, 3 minutes. Wash in water. Blot, dehydrate, and differentiate in aniline oil until pink colour returns. Clarify in Xylol and mount in Xylol Balsam. This method is preferable to the Gram-Eosin method, as aniline oil is more gentle in decolorising action than the alcohol used in the latter.

For Jensen's Modified Gram's Method using stronger Iodine Solution and Neutral Red as counterstain.

A simple stain for sections is :—

Carbol Thionin Blue.—Thionin Blue, 0·65 Gm.; Absolute Alcohol, 3·5 Cc.; Phenol Solution, 5% 39 Cc.

Carbolic Methyl Violet. *Syn.* Carbol-Gentian-Violet.

This is better than Aniline Gentian Violet especially in hot climates. The Methyl Violet Stain is:—Melted Carbolic Acid 12·5 Cc., Absolute Alcohol 25 Cc., Methyl Violet 6 B. 1 Gm. Dissolve, keep in a warm place 24 hours and filter. Fix the smear with Alcohol. Place 3 or 4 drops of Distilled Water on the smear and one drop of the stain. Then Gram's solution in the usual manner. Counterstain with Safranin or weak Fuchsin.—B.M.J.E. /13,96.

Aniline dyes exhibiting the most powerful lethal action on a typically Gram + staining micro-organism (*Staphylococcus*) are those which can be used with the greatest success by the method. Substances having special affinity for the dyes in question are assumed to be present in Gram + staining organisms and as Iodine plays a special role in the Gram reaction, special examinations with *lipoid* substances gave interesting data. (1) Treatment of *B. Coli* with Lecithin Emulsion may make it Gram + staining. Boiling *Staphylococci* with Ether renders them almost entirely non-Gram staining.—Jl. Path. & Bact.—July, 1911, p. 146.

We found that non-Gram staining organisms were decolorised in periods varying from 2 to 5 minutes, *using strong Methylated Spirit*, and that Gram staining organisms were not decolorised even after one hour's washing. If weaker spirit, *e.g.* 60%, is used, organisms that were not decolorised in an hour with strong spirit may be almost decolorised in ten minutes, therefore the *strongest Spirit is absolutely necessary*. The Iodine treatment should be for at least 5 minutes, in fact it cannot be overdone in a film preparation. We should recommend 10 minutes washing with the spirit. See also gonococcus chapter.

List of some pathogenic and common non-pathogenic organisms stained and not stained by Gram's method :—

GRAM +	GRAM —
All cocci except.....	Gonococci. Meningococci. Micrococcus Pharyngis Siccus. " flavus. " Melitensis. " catarrhalis.
All diphtheroids.	The whole Coli-Typhoid group; Typhoid, dysentery, paratyphoid.
All spore-bearing aerobes :	<i>B. faecalis alkaligenes</i> , and capsulated group; <i>Pneumobacillus</i> , <i>B. Proteus</i> , and non-pathogenic vibrio group.
<i>B. Subtilis</i> , <i>B. anthracis</i> , <i>B. mycoides</i> and anaerobes, <i>e.g.</i> , <i>B. Tetani</i> , <i>Welchii</i> , <i>Sporogenes</i> , etc.	Chromogenic bacteria, <i>e.g.</i> , <i>B. pyocyaneus</i> .
Streptothrix and Tubercle group.	Hæmorrhagic septicaemic group, <i>e.g.</i> plague.
All moulds.	Hæmoglobinophilic group, <i>e.g.</i> , influenza.
All yeasts.	Glanders.

Nitrobacterin.—Nitrifying bacteria on the nodules of leguminous plants (peas, beans, clover, &c.) have been cultivated under this name for enriching soil. The sequence of crops is turnips, barley, clover, wheat. Alkalinity of the soil is a *sine qua non* for the growth of bacteria which produce acid in their proliferation.

Semen Test.—The presence of spermatozoa may be detected by evaporating a drop of the liquid from the moistened stains, fixing it by a flame and staining with eosin and methyl green. At the base of the head of the spermatozoon is a hemispherical portion which stains green, while the anterior part and tail stain red. Some prefer the use of methyl green alone. Ehrlich's Hæmoxyl (stain 5 minutes) wash in distilled water, then in tap water until blue, and counterstain with Eosin solution (2 or 3 minutes), also gives good results. The following has been successful in 85 to 90% of cases in medico-legal practice in India : soak the piece of cloth for a few minutes, scrape off film on

to a slide, spread out, dry in air, and fix over flame. Cover with Carbol-Thionin, wash after a few minutes with distilled water and drain. Dry and examine with $\frac{1}{2}$ -inch oil immersion. The middle portion of the spermatozoa stains more deeply and has semi-lunar shape.—S. Mallarmah, Analyst, '52,399, per P.J. ii./27,273.

Semen Stains may be identified by boiling (fabrics) 2 minutes in watery solution containing Tannin $\frac{1}{2}\%$ and Sulphuric Acid 1 per 1,000, then wash with strong Ammonia Solution 1 in 400 for 2 minutes, immerse 5 minutes in a solution of Potassium Bichromate 1 in 10,000 with 1 in 1,000 Sulphuric Acid, transfer for 2 minutes to 2% Potassium Cyanide Solution; finally rapidly wash in distilled water. Scrape and tease up on a slide, dry, and stain.—B.M.J. ii./06,1261,1843.

Semen Stained by Eosin.—Cut a portion of the cloth $1 \times 1\frac{1}{2}$ inches, soak in Müller's Fluid 24 hours preferably at 37° C. in incubator (*e.g.*, covered watch glass). Wash in several changes of water to remove dirt and also fixing fluid. Place the cloth, one end held in forceps, for a moment on blotting paper to remove excess of moisture, then lay flat on centre of micro slide. Pass edge of scalpel or of another slide with a fair amount of pressure from the end of the cloth fixed by the forceps, to the other. Repeat on the other surface, turning the cloth over on the same portion of the slide. The end of the cloth is then placed, with the forceps between finger and thumb, the rest being pleated up by the same means and tucked in so that firm pressure of the tips of forefinger and thumb causes a drop of liquid to fall which add also to the slide. Dry in incubator, and stain three minutes with 1% Eosin solution.—B.M.J. ii./08,501.

Picric Acid Test for.—Mix the suspected semen, whether liquid or dry, with a little water, add a drop of Glycero-Solution of Picric Acid containing a little alcohol—if human semen, yellow needle crystals, visible under the microscope.

Preparation of Sections before Staining.

Rapid Paraffin Method for small pieces of tissue. Fix in 10% Formalin 1 hour, 70% Alcohol 1 hour, 95% Alcohol 1 hour. Absolute Alcohol $\frac{1}{2}$ hour, Xylol $\frac{1}{2}$ hour, in incubator at 37° C. in each case, and Paraffin $\frac{1}{2}$ to 2 hours at 55° C.—Stitt.

Slow Paraffin Method.—Fix in Alcohol (not Formalin) 2 days, then place in Xylol 3 to 5 days.

Rapid Gum-freezing.—Place tissue into boiling Müller's Fluid or Formol-Müller, or plain water. Boil 3 minutes, wash in water; freeze in Gum with Ethyl Chloride or by Carbon Dioxide.

Zenker's Fluid.—Bichromate of Potassium 2.5 Gm., Sulphate of Soda 1 Gm., Corrosive Sublimate 5 Gm., Glacial Acetic Acid 5 Cc., Distilled Water 100 Cc. The Glacial Acetic Acid is added only just before fixing.—Stitt.

Müller's Fluid.—Potassium Bichromate $2\frac{1}{2}$, Sodium Sulphate 1, Water 100. Used in histology for hardening tissues.

Formol-Müller Fluid.—Müller's Fluid 100, Formalin 5

Transparent method for bony specimens.

Dehydrate in successive baths of Alcohol and Acetone, Anilin Oil, Xylol, and Liquid Paraffin.

Formalin Preservative Solution.—Formalin (40%) 78, Potassium Acetate 3, Potassium Nitrate 1, Glycerin 40, Water 140.

This has the advantage of retaining the colour of pathological specimens. Method of cutting frozen sections of fresh tissues for immediate microscopic diagnosis during operations. Lockwood & Shaw.—B.M.J. i./07,127.

Frost's Solution for preserving anatomical specimens. Sodium Fluoride 80, Chloral Hydrate 80, Potassium Acetate 160, Cane Sugar 3,500, Saturated Thymol Water 8,000. The specimens retain life-like appearance. L. i./12,579.

Farrant's mounting medium.—Gum Acacia 32 ozs., wash well with 100 ozs. of water in two or three lots and dissolve in 40 ozs. of boiling water with constant stirring. Strain through muslin and add Arsenious Acid 1 drachm in Glycerin 40 ozs., heat gently to clarify.

Apathy's Gum Syrup. For ringing Slides.—Picked Gum Arabic 50, Cane Sugar (ordinary, not candied), Distilled water, of each 50 Gm. Soak in water, and add 0.05 Gm. Thymol. Render alkaline with a little Sodium Carbonate. This sets in about 15 to 30 minutes in a warm room.

The use of this with other precautions, helps in preventing slides from fading.—L. i./11,877.

A method of neutralising the disagreeable odor arising from pathologic specimens. The Formaldehyde-preserved material is rinsed in water and dipped in a solution of very dilute Ammonium Hydroxide, made up by adding 5 to 10 Cc. strong Ammonia water to a litre of tap water. The Ammonia combines readily with Formaldehyde to form Hexamethylenamin. The mixture smells faintly of Ammonia, but completely deodorises Formaldehyde-saturated tissues.—J. C. White,—Jl. A.M.A. ii./25,436.

CULTURE-MEDIA FOR BACTERIOLOGICAL INVESTIGATION.

Nutrient Broth.—Boil 'Lemco' 5 Gm., Peptone 10 Gm., Sodium Chloride 5 Gm., Water 1,000 Cc. Make faintly alkaline with dilute Sodium Carbonate solution, using litmus as indicator, and filter through grey paper. The broth thus prepared may be run into specially cleaned test-tubes, about 5 Cc. into each. These are now plugged and sterilised at 100° C. for a quarter of an hour on three successive days, or the broth may be converted into other nutrient media.

The following is sometimes used:—Beef (or horse, &c., flesh) 450 Gm. freed from fat and minced, is extracted for twenty-four hours with cold water 1,000 Cc. The albumin is coagulated by heat and strained off. The resulting extract is boiled ten minutes with Sodium Chloride 5 Gm., and Peptone (in powder) 10 Gm., with occasional shaking. Finish as above after rendering alkaline.

Standardisation.—The broth and the gelatin and agar media made from it are acid to phenolphthalein, but are frequently neutral or even alkaline to litmus—this latter not being sensitive to many of the weak organic acids present in the meat extract. The medium is, therefore, standardised with $\frac{N}{10}$ soda in the presence of phenolphthalein. The reaction of a medium is usually expressed by the number of Cc. of normal alkali required to be added to 1 litre of medium to render it exactly neutral to phenolphthalein, e.g., +10 indicates that 10 Cc. of N soda have to be added to neutralise it. *This reaction has been found best for general bacterial growth, and is the standard employed.* The rule for standardising, therefore, is to subtract 10 from the number of Cc. of normal soda that must be added per litre; for example, if 10 Cc. of a medium require 1.2 Cc. of $\frac{N}{10}$ soda, then 1,000 Cc. = 12 Cc. $\frac{N}{1}$ soda. The medium is now neutral to phenolphthalein, but distinctly alkaline to litmus. Then subtracting 10 Cc. from 12 we have 2 Cc. of $\frac{N}{1}$ soda to be added to 1 litre of medium.

Media are now generally standardised by adjusting to a definite Hydrogen-ion concentration, using indicators.

Glucose Broth consists of Nutrient Broth with the addition of 1 or 2% of pure anhydrous glucose added after final filtration, but prior to sterilisation.

Glycerin Broth.—Nutrient Broth containing 5 to 8% of Glycerin.

Litmus Broth consists of the addition of a sufficient quantity of Litmus solution to neutral broth to render it distinctly blue in colour.

Nutrient Gelatin.—Broth 1,000 Cc., gelatin 125 Gm. Melt in steamer and clarify by adding the white of one egg, to which a little water may have been added, render faintly alkaline, place in steamer to make quite hot, and filter in the same, leaving the portion containing the coagulated albumin, which will have subsided, carefully until the last. Run the medium into tubes, about 5 or 8 Cc. into each according as to whether 'slopes' or 'stab' preparations are required. Sterilise on three successive days.

Glucose Gelatin consists of nutrient gelatin to which 1 or 2% glucose has been added after filtration. For the cultivation of anaerobic organisms and to observe gas formation. Must not be sterilised in the autoclave.

Nutrient Agar.—For this medium the following gives satisfactory results:—Nutrient broth 1,000 Cc., powdered agar-agar 20 Gm. (passed through a drug-mill and made as fine as possible); melt in the steamer, or better in an autoclave, allow to cool slightly, or, if time is an object, cool by shaking under a stream of cold water from the tap; add white of two eggs, *make just alkaline*, boil in the steamer or autoclave twenty minutes, and then transfer to a tall beaker; allow to get quite cold, remove the solid mass from the beaker, and

cut off the bottom of the block of jelly containing the coagulated album and sediment. The remainder is again thoroughly melted in the autoclave steamer, and will then filter well (in the steamer). It may be poured in tubes, and sterilised in the autoclave for a quarter of an hour under a pressure of at least two atmospheres—or, in the steamer on three successive days. Instead of cutting off the sediment on setting, it may be kept out by straining the hot liquid through butter-cloth previous to filtration.

N.B.—The white of egg should be added when the medium has almost set—i.e., as cool as possible—as the albumen coagulates at 65° C. and it acts purely mechanically by carrying down with it the particles of suspended matter.

Neutral Red Egg Medium (Fleming's) for cultivation of Staphylococcus from the urine. Differs only from Dorset's in that it contains 0.005% Neutral Red as an indicator.

Dorset's Egg Medium.—The contents of 4 fresh eggs are well beaten and 25 Cc. of water added. The mixture strained through muslin to remove air bubbles, then tubed (or plated) and heated 4 hours at 70° C. It may be further sterilised by heating in the autoclave for 5–10 minutes at 105°. The addition of sufficient basic Fuchsin to colour the medium slightly pink enables early growths to be more easily seen.—M. & R.

H. Warren Crowe's procedure for the preparation of Neutral Red Egg Medium is as follows:—He places the requisite amount of Neutral Red (25 Cc. of 0.01% aqueous solution of Neutral Red for each egg) in a flask plugged with wool, and autoclaves it together with two rubber corks, one with two wires or glass rods long enough to reach within one inch of the bottom of the flask, the other carries two tubes, a short one reaching two or three inches from the cork on the inside and fitted with a hooded pipette on the outside and one reaching to the bottom of the flask, the outer portion being bent to form a recurved angle and plugged with wool. He then soaks the eggs in spirit, flames them and cracks them at each end with long sterile sinus forceps, breaking the yolk by pushing them in and opening them inside the egg. When all the eggs are in, the rubber cork with the rods is placed in position and the contents of the flask emulsified by shaking (the rods serve this purpose). The flask is then inverted, suspended and allowed to stand until the whole of the particles of egg-shell, etc., have settled below the level of the short tube. The medium is then ready to run into tubes or plates, which are finished by heating to 90° C. for half an hour.—P.R.S.M., Path. Sect.—Vol. V. p. 117; L. i./13, 77.

Musgrave's Medium.—Beef Extract 0.5, Sodium Chloride 0.5, Agar 20, Tap Water to 1,000. Alkalinity minus 1 gives a growth of fairly constant characters. Employed in growing coli-form bacilli from patient's boy in making autogenous vaccine (for treating goitres).—L. i./13, 1371.

Blood Agar is prepared by streaking nutrient agar with blood drawn under the strictest aseptic precautions from the finger, or from a freshly killed animal. It may be used in the 'slope' form or as plates. The gonococcus grows favourably on this medium.—N.B.—For Gonococci and Pneumococci use the patient's blood if possible. See also *B. Influenzae* Fleming's Method.

Endo's and Hiss' Medium, *vide* p. 608.

Chocolate Medium.—Bullock's Blood Trypsin—Agar (H. W. Crowe). For Meningococcus, see *Cerebro-Spinal Fever*, Vol. I., p. 911.

Citrated Media.

The growth of the cholera vibrio in broth is markedly increased by addition of a small quantity of *Sodium Citrate*. The growth of *B. paratyphosus* A is inhibited whilst that of the three strains of *B. paratyphosus* B also of *B. paratyphosus* C is enhanced. Decomposition of the citrate in the case of *paratyphosus* B and C is clearly shown by a reduction in the volume of the precipitate on addition of lead acetate, and forms a means of discrimination between *B. paratyphosus* A on the one hand and B and C on the other, for in the case of the two latter the amount of precipitate with the lead acetate is considerably less than in the case of *B. paratyphosus* A. Further *Friedländer*, *B. Cloacæ* and *B. paratyphosus* C produce gas in fluid citrated media without addition of any carbohydrate, for 72 hours or more. Citrated media can be autoclaved. A full list of organisms which are enhanced and decreased is provided.—H. C. Brown, L. i./21, 22.

Glucose Agar consists of nutrient agar to which 1 or 2% glucose has been added after filtration. In the upright form is used also for deep stab cultivations of anerobic bacteria. Must not be sterilised in the autoclave.

Glycerin Agar is nutrient agar with the addition of 5 to 8% of glycerin. Is a satisfactory medium for the growth of *Bacillus diphtheriæ*, *B. tuberculosis* and *Streptothrix actinomycosis*.

Maltose Agar.—Maltose 12, Peptone (in powder) 3, Agar 3.9, Water 300. This is prepared in the customary manner, but the product is not neutralised. Blaxall's formula is Maltose 12, Peptone 1½, Agar 9, Water 300 For ringworm cultivation.

Peptone-water (Dunham's Solution).—Peptone 5 Gm., sodium chloride 10 Gm., tap water 1,000 Cc.; boil in the steamer one hour, filter, and sterilise. Not necessary to render alkaline. Used for the production of the indol reaction as one of the aids, for example, to distinction of *B. typhi abdominalis* and *B. Coli*. It was originally utilised for cholera-diagnosis.

Casein as a substitute for Peptone for bacterial culture. The amino-acids required are produced by tryptic digestion of Casein (Lait proto, No. 6). Standardisation is effected by employing phenol-sulphone-phthalein solution. The broth is cheaper than peptone and is of constant composition. It is useful for making into Agar culture medium and for special media, e.g. Endo's, etc.—S. W. Cole & H. Onslow, L. ii./16,9. See also Cole & Onslow's Tryptic Agar.

Potato.—Cut into 'half-cylinders' with a potato-borer. Pieces soaked overnight in water to wash off excess of starch. Wide test-tubes (1 inch by 6 inches) are plugged and sterilised, and a little distilled water is placed with each half-cylinder in the tubes. The water prevents drying up in sterilising, which is effected by heating on three successive days. Must not be sterilised in the autoclave.

Milk—The cream is skimmed from cows' milk, and the resulting 'skimmed' milk sterilised in the steamer for ½ hour on three successive days.

May also be drawn direct by means of a catheter into sterile vessels with the aseptic precaution. Organisms are said to grow better in this than in milk which has been heated.

Litmus Milk.—The above—with a small proportion of Litmus solution added. Used for detection of acid formation.

Phenol Red Milk preferable to Litmus Milk and sugar media, e.g. for *B. paratyphosus*.—H. C. Brown, L. i./22,842.

Blood-serum.—The serum is separated from fresh blood obtained from the jugular vein of the sheep. It is centrifugalised and filtered through a sterile Chamberland filter. (The candle is heated in a muffle-furnace, or in a bright fire, if it has been previously used for the same purpose.) The filtrate may then be poured into sterile test-tubes, plugged—and inspissated, first at 80° C., then at 60° C., and the latter temperature is maintained eight to twelve hours, or more if necessary. The medium is finally tested after capping by incubating at 37° C. for twenty-four hours to ensure sterility.

Löffler's Blood Serum.—This consists of ordinary 'Serum' 3 parts mixed with neutral peptone bouillon 1 part with 1% grape sugar added to it. Tubes are filled and sterilised as under Blood Serum.

Elschnig's Medium is a fluid one in which reliance is placed for detecting pneumococci. It consists of 1 part of Horse Serum and 3 parts of bouillon without Peptone.

Sterilisation of Serum by adding Chloroform 0.5% with addition of heat—one hour at 45° C. in stoppered bottles. Useful method for making Blood Agar, Serum Agar, etc.—P. Fildes, L. i./17,492.

Boeck's Locke Egg-Serum Medium (L.E.S. Medium).

Wash four eggs, brush with Alcohol and break into a sterile flask containing glass beads: add 50 Cc. Locke's solution. Fill test-tubes sufficiently to produce slants of 1 to 1½ inches on coagulation by heat. Slant tubes in an inspissator and heat at 70° C. till egg mixture is solid. Transfer to autoclave and sterilise for 20 minutes at 15 lbs. pressure. Add to each tube a mixture of 8 parts sterile Locke's solution and 1 part inactivated human serum till liquid reaches 1 cm. above egg slant.

A modification is the L.E.A. Medium of Boeck and Drbohlav, the diluted serum being replaced by 1% solution crystallised egg albumin in Locke's

solution, sterilised by filtration through a Berkefeld filter: another modification is the replacing of the egg slope by a blood-agar slope. The reaction of these media should be pH = 7.2 to 7.8.

Used for the cultivation of *E. histolytica*, *E. coli*, *E. gingivalis*, and all the intestinal amœbæ of man, as also other human flagellates.—Wenyon, 1298.

Noguchi's Serum Medium.

Has the following formula: Saline solution 0.9% 800, fresh rabbit serum 100, Nutrient Agar (2%, pH = 7.2) 100, and rabbit hæmoglobin solution (part defibrinated rabbit's blood in 3 parts distilled water) 10 to 20 part. For cultivation of spirochetes of Weil's disease and relapsing fever, also for various species of leishmania, growth occurring on the top of the medium as a whitish cloud or scum.—Wenyon, 1304.

Ponselle's Medium.

Sodium Chloride 0.3 to 0.8 Gm., Witte's Peptone 2 Gm., Gelatin 2 Gm., normal Sodium Carbonate solution 1 Cc., Distilled Water to 100 Cc. Heat rapidly on water-bath and sterilise in autoclave at 110° C. for half an hour. Cool to laboratory temperature and add equal volume of rabbit's serum, when medium for primary culture is required, and defibrinated rabbit's blood for subcultures. Distribute in quantities of 3 Cc. in test-tubes and inactivate by keeping for half an hour at 56° C. For cultivation of pathogenic trypanosomes. The Sodium Chloride content varies with the trypanosome, being 0.3 Gm. for *T. brucei*, 0.6 Gm. for *T. pecaudi*, and 0.8 Gm. for *T. rhodesiensis* and *T. dimorphon*.—Wenyon, 1305.

Trypsinised Blood Egg Medium (Wang.)

Trypsinised defibrinated ox blood (fresh) 10 parts, ditto plain bouillon 10 parts, ditto plain milk medium 4 parts, beaten whole egg 10 parts. After trypsinisation, the three fluids are well mixed with the beaten egg and the whole strained through gauze or muslin. Tubes are sloped in an inspissator so heated as to take 3½—4 hours to reach 75° C.: leave at that temperature for 15—30 minutes and autoclave at 120° C. for 20 minutes. Trypsinisation is carried out by adding Liquor Pancreaticus (Benger) 0.2 Cc. to 10 Cc. blood and allowing the tubes to stand 24 hours at 37° C.

Tubercle bacillus grows rapidly at body heat. Pneumococcus grows very rapidly and growth far surpasses that obtained on other media. Streptococcus thrives extremely well. Diphtheria bacillus develops readily—12-hours after incubation colonies are more numerous than with Löffler's serum. Also favourable for meningococcus, hæmophilic bacilli, and the bacilli of glanders and plague.—C. Y. Wang, L. ii./28,447.

Preserving micro-organisms.

A modification of Ungermann's method for keeping pathogenic bacteria alive for considerable periods without sub-culturing is described. Tubes of Legroux's Formalised Serum, each covered with a layer of Vaseline Oil, are used. Many organisms such as meningococcus, gonococcus, cholera vibrios, etc., difficult to keep in the ordinary way, have been preserved for periods from 4 months to 2 years.—C. Fruche, Ann. Inst. Pasteur, '24,38, p. 516, per J.C. A. i./24,1013.

For other media described in the Text consult the Index.

EMBALMING.

If it is impossible to make the autopsy at once, preservative may be injected into the body until such time as convenient; about 300 Cc. of 5% solution of Formalin suffice. It is introduced through the arteries (arterial embalming) or a coarse trocar and cannula may be driven deeply into the tissue and the cavities and organs injected (cavity embalming).

Perchloride Embalming.—The former method is usually practised by opening one of the large superficial arteries, as the femoral, and forcing the fluid through the vessels. Nauwerck uses the following—500 Cc. injected by syringe; long cannulæ of different calibres, with pear shaped ends and with stopcocks or, preferably, with double stopcocks; strong twine; scalpel, scissors, forceps, grooved director, hæmostats, an aneurism-needle, and ordinary needles; basins and buckets; several packages of absorbent cotton cloths and sponges; and 10 litres of a 10% solution of mercuric chloride. The method of embalming is begun by exposing the lower part of the abdominal aorta and the two iliac arteries. Two ligatures are placed beneath the aor

about two finger-breadths apart, and the aorta is obliquely incised to allow the entrance of the cannula, which is secured by tying the distal ligature over it. The injection into the upper part of the body is then begun carefully and slowly, pausing occasionally when the counter-pressure becomes too great. About 3 litres are injected or less, depending upon the appearance of swelling of the face, seen first about the eyes and chin. The cannula is removed, both proximal and distal ligatures are tied, and the aorta is cut through. In like manner a litre of the solution is injected into each leg through the common iliac artery. A cannula with a double stopcock can be used to inject both the upper and lower parts of the body at the same time. The mesentery is ligatured, and the intestines, from the beginning of the jejunum to the end of the sigmoid flexure, are removed, opened, washed out, and put in a 1% solution of mercuric chloride, and later replaced in the abdominal cavity, wrapped in sublimate wool, or where practicable, disposed of by cremation. The stomach, duodenum and rectum are cleaned out with sublimate solution and packed with sublimate wool. The bladder, vagina, external ear, and nose are similarly treated. The abdominal cavity is carefully wiped with a cloth wrung out of the perchloride solution and dried, and the abdominal incision is sewn up. The surface of the body, with the exception of the hair, is also wiped with the solution and dried. If this method fails, Nauwerck injects into the carotid and axillary arteries.

Formalised Arsenical Embalming Injection.—Hewson recommends the following injection for embalming—Sodium Arsenate 40, boiling water 157. Boil until dissolved and add glycerin 40, formalin 2 or 3. About 2 and one-half gallons are introduced into an artery—say the common carotid—by gravity, openings having been previously made in the toes or in several of the veins if they be distended with blood. After the injection the body is thoroughly greased, covered with paper, bandaged and placed in cold storage until wanted for dissection. *Caution*—These solutions are caustic in action on the hands.—Cattell's Post-Mortem Pathology.

PROPRIETARY MEDICINES.

In the following list we provide the approximate composition of Proprietary Medicines—several are mentioned incidentally in the text. The '*British Medical Journal*,' the '*Lancet*,' etc., have from time to time published results of analyses, and reference to their pages is made below in each instance. Considerations of space have usually obliged us to mention only the ingredients which have undoubted therapeutic effect. The reader is referred to the original sources for further details. With regard to the great majority of medicines, it should be noted that there are other ingredients which, though for the most part flavourings or colourings, may in some cases be considered to be medicinal. Our list must not be considered complete, though care has been exercised to state therein what appear to be the chief ingredients. The composition of some Proprietary Medicines may be found to vary from time to time. Again the composition of a proprietary article in one country does not necessarily convey a correct impression of articles sold under the same name in other countries.—B.M.J. i./10,339. The majority of those to which we give B.M.J. references were described in '*Secret Remedies, what they cost and what they contain* (1909),' and in '*More Secret Remedies* (1912),' issued by the British Medical Association, but the works are out of print. In some instances we give these books as our only references.

The composition of a number of Proprietary Medicines as offered for sale in Italy are taken from L. i./24,256.

Comparison of conditions of Sale of Patent Medicines in various countries.—L. ii./12,1672. See also 'The Law in Foreign Countries' in the 1914 *House of Commons Select Committee on Patent Medicines Report*, reprinted as a supplement to the *Lancet* on 'Sale of Patent Medicines' Jan. 10, 1925. This deals with the present position in The United Kingdom, the British Dominions, Germany, Austria, Hungary, France and Italy.

Australian Practice.—Wording respectively permitted and not allowed in advertisements and descriptions of proprietaries.—C.D. i./13,912; B.C.D. i./13,564.

New Zealand QUACKERY PREVENTION ACT, 1908—any person commits an offence who publishes any statement intended to promote the sale of any article as a medicine for prevention or cure of any ailment or physical defect which is false in any material particular.—Gadd.—B.M.J. i./11,767. We understand, however, that there is a provision in the Act that action can only be taken by Government permission which distinctly detracts from the utility of the measure.

Desirability of enforcing the labelling of Proprietary Medicines and Foods with a full statement of contents as required by the Pure Food and Drugs Act in **America**.—‘State Regulation of Proprietary Medicines and Foods.’—B.M.J. ii./08,574.

The American Medical Association drew up regulations for controlling trade names of pharmaceutical and chemical preparations and issued same to manufacturers of medicinal products.—Chicago, March 15/1912.

U.S.A. Proprietary Medicines.—The Department of Agriculture through the Bureau of Chemistry has issued details as to Claims of Therapeutic Effects, Indefinite and Sweeping Terms, Testimonials, etc., for guidance as to wording of labels permissible under an Amended Food & Drugs Act. The names, e.g. “Nerve Tonic,” “Lung Balm,” “Kidney Pills,” are objected to. “Guarantees” as to refund of money also not permissible.—B.M.J. i./15,24.

In **Germany** Patent Medicines are in great demand.—L. ii./26,1027.

Patent Medicines and Revenue.

Revenue from Patent Medicine Stamps is £1,125,000 a year, which means that something like 500,000,000 packets of patent medicine are sold in England, Scotland and Wales.—P.J. ii./24,563.

The Inland Revenue Authorities hold that an advertisement in a technical journal which does not go to the public does not constitute an advertisement to the public.—C.D. i./13,928.

Dr. Cox, before the Select Committee on Patent Medicines (1912) made the statement that £2,500,000 had been paid by the public since 1908 on Patent Medicines.—C.D. i./12,923.

“The Government reaps a very rich harvest from secret preparations. They have a Government stamp on them, and the Treasury gets many thousands a year out of them,—wrongly, I think. The Government does not think so, however.”—Coroner Dr. F. J. Waldo.—P.J. ii./09,303.

Administration of Adulteration Laws.—Sale of Food and Drugs Acts with regard to Proprietary Medicines,—they affect these articles very little. Legislature to make a fresh start and create a new body.—A. W. J. MacFadden, Chief Inspector of Foods under L.G.B.—P.M.C.E., C.D. i./13,874.

In B.M.J. of May 27th, 1911, papers on ‘Cancer Credulity and Quackery’ (see also Cancer Chapter), ‘Bone-setting,’ ‘Quackery and Female Complaints,’ ‘Skin Diseases and Cosmetics,’ ‘Unqualified Practice,’ ‘Quackery in Rural Districts,’ ‘Quackery in the Past,’ ‘Herbalists and Medical Practice,’ ‘Unqualified Practice in the Eye of the Law,’ ‘Unqualified Practice through the Post,’ ‘Quackery in Aural Diseases,’ ‘Quackery in France,’ ‘Causes of Quackery,’ etc., will be found.

The House of Commons appointed a **Select Committee to Enquire into the conditions prevailing in the United Kingdom regarding sale of Patent and Proprietary Medicines**. The Royal College of Physicians, London, made certain recommendations as to the exact composition of the contents of bottles, etc., being printed thereon, and that manufacturers shall not be allowed to print names of diseases or symptoms on same. cf. C.D. July 1, 1911.

The Committee met for the first time May 9th, 1912, and received evidence from the Board of Inland Revenue (per Sir N. Highmore) also on May 16th, 1912.—cf. B.M.J. (May 18th) i./12,1140; C.D. May 18th, 1912.

Subsequently numerous meetings were held and a large number of persons were examined. We have embodied the evidence where of sufficient interest under the appropriate headings.

The **Report of the Committee**, issued Aug., 1914, obtainable from Wyman & Sons, Fetter Lane, E.C., found that the existing law offers no check to gross abuse of the public and **recommended** that the administration of the Law governing the advertisement and sale of patent, secret and proprietary medicines be part of the functions of the Ministry of Public Health.—P. J. i./14,346; C.D. ii./14,339; cf. L. ii./14,653,702.

After long and careful consideration, the Committee reported that the **exhibition of formula**—a much discussed proposition—(except in the case of alcohol, poisons and certain dangerous drugs) does not appear to us to be a proper, practical or effective measure." Further, that pure drugs, **vended entire under fancy names, should no longer be exempt from duty.** The distinction between the name of an ailment, and the name of an organ, the seat of that ailment, should be abandoned, and the exemption of medicines generating Carbonic Acid Gas should be omitted.

Any reference in advertising matter to the *Government Stamp* should be prohibited and no name of a proprietor or firm should be printed on the stamp.

An **"Index and Digest of Evidence"** of the Report was issued officially (Wyman & Sons, Ltd., 11*d.*). It is a summary of the Report.

A patient cannot 'patent' a prescription he receives from a consultant. The patent would not be valid, as the patient would not, for one thing, be the "true and first inventor" of the prescription.—E. J. Parry,—P.M.C.E., C.D. i./13,560.

Difficulties of Analysis.—Arnica, Bryonia and Buchu have medicinal effect, but science has not been able to state what the active principles are,—these cannot be discovered with certainty by the analyst. Gentian, Mezereon Hamamelis, Rhubarb and Senna have medicinal effect—in some cases science does not know why. When mixed together it is almost impossible for an analyst to identify them.—P.M.C.E., C.D., July 6/12, Ind. fol. 23.

Six minims of Ipecacuanha Wine in a six-ounce bottle of water would not be detected by an analyst unless he were put on the track.—P.M.C.E., C.D., July 6/12, Ind. fol. 23.

Medicated Wines.—Necessity of stating Alcohol strength on the labels—it is often greater than that in light wines.—Dr. Mary Sturge, P.M.C.E., C.D. i./12, Ind. fol. 5.

'Registration' foreshadowed—disclosure of ingredients of preparations to a Government Department might be an advantage to the manufacturers as giving more definite public recognition.

International Pharmacy.—French regulations bearing on the introduction of foreign pharmaceutical preparations are exceedingly severe. The reciprocity is too one-sided!—B.M.J. i./19,534.

Foreign-made goods.—Need for careful description.

A series of notices has been issued by the Board of Trade calling attention to breaches of the **Merchandise Marks Act**, which is not being satisfactorily complied with in some cases. An article of foreign manufacture must be stamped with the country of origin (1) when it is one as to which an Order in Council has been made, (2) **when it bears an indication which may suggest British origin, e.g., the name of a British agent.**—P.J. ii./28,545.

Proprietary Medicines Bill.

Introduced into the House of Lords, July, 1920, for the purposes *inter alia* of:—prohibiting the sale or advertisement of remedies purporting to treat or cure certain diseases, registering all proprietary medicines and their owners, and disclosing the formulæ of such preparations. Proprietary Medicine means any medicine held out by advertisement, label or otherwise in writing, as efficacious for the prevention, cure or relief of any malady, ailment, infirmity or disorder affecting human beings and

(a) Which is sold under a trade name or trade mark to the use of which any person has or claims or purports to have an exclusive right; or

(b) Of which any person has or claims or purports to have the exclusive right of manufacture or for the making of which any person has or claims or purports to have any secret.

A considerable amount of discussion has taken place on the subject of this Bill, and the expressions of opinion seem to have been more on the side of pharmacists than on the side of the medical profession. The following are a few brief abstracts from recent journals, in particular from the "Chemist and Druggist."

At a meeting of chemists a pharmacist expressed the opinion that the Bill is one of the most serious menaces to the liberty and privileges of pharmacists that have ever been devised.—C.D., Oct. 16/20. The speaker stated further that pharmacists should obviously support legislation in so far as it will prevent fraud in the proprietary medicines trade but not to the extent of depriving chemists of their legitimate rights in the sole interest of the medical profession. The imposing of registration fees upon retail chemists would be a serious matter.

Exception has been taken throughout the discussion to the disclosure of the ingredients and the proportions of the same in proprietary remedies.

In the C. & D. of Oct. 23/20, is an analysis of the provisions of the Bill as amended in the Committee of the House of Lords, together with numerous suggestions for further amending the Bill. No useful purpose would be served by including here details of penalties, definitions, things forbidden, and so forth, also the list of diseases (cancer, consumption, fits, epilepsy, etc.) contained in what is known as the Major Offence Clause II., as the exact data with regard to contravention of clauses have not been settled. See also C.D., Oct. 30/20 and Jan. 8/21.

Details of Evolution of the Stamp Acts.—S. W. Woolley, C.D., Dec. '20, 1770 J.

The Bill as amended in Committee of the House of Lords together with the 1914 Committee Report has been printed as a special supplement to the *Lancet*.—Jan. 10, 1925.

Prof. Clark recalls the Stevens Consumption Cures and other matters.—B.M.J. ii./23,941.

Patent Medicine Duty—Parliamentary Discussion.—B.M.J. ii./27,43.

Draft Regulations of Proprietary Medicine Control in Australia. These proposed Regulations are more drastic than those contemplated by the British Committee of 1920.—P.J. ii./27,453.

Concession by Commissioners of Customs and Excise.

Manufacturers of Proprietary Medicines may supply to either Chemists or Doctors such preparations unstamped for dispensing only. These may be dispensed without mixing with other drugs. Manufacturers must make application and keep records. No advertising matter allowed. The form of the article must differ.—May 28, 1929.

Venereal Disease Act 1917—provisions of, see Vol. I.

PROPRIETARY MEDICINES, WITH REFERENCES.

The author has data concerning a number of Proprietary Remedies which have been examined in his laboratory during years past and will be pleased to place the information at the disposal of medical men on receipt of enquiry. The following list is now abbreviated, many having apparently gone out of fashion.

*It has not been thought necessary to add the T.M. Nos. in this chapter, but the files have been consulted at the Patent Office on going to press to determine that the Marks are on the Register.

Ambey's Salt.—(Aperient) Tartaric Acid, Sodium Bicarbonate, Magnesium Sulphate and Sugar—L. ii./03,1493.

***Albert's Grasshopper Pills.**—Barb. Aloes 0.12; Colocynth, 0.04, Jalap Resin 0.02, Powdered Ginger 0.006, Hard Soap 0.03.—L. i./24,256. (As sold in Italy.)

***Albert's Grasshopper Ointment.**—Olive Oil 30, Palm Oil 180, Coloph. Res. 270, Yellow Wax 60.—L. i./24,256. (As sold in Italy.)

***Allen's Antifat.**—70 minims liquid extract of Fucus in the ounce.—B.M.J. ii./07,209.

Allen's *Foot-Ease.—Salicylic Acid 5, Boric Acid 45, Magnesium Silicate 50.—L. i./24,256. (As sold in Italy.)

***Angier's Throat Tablets.**—Slippery Elm Bark 1.0, Licorice 0.02, Ext. of Coltsfoot 0.03, Liquid Paraffin 0.15.—L. i./24,256. (As sold in Italy.)

* **Antexema.**—Soft Paraffin 35.4, Boric Acid 1.5, Gummy Matter 12.4, Water 50.7.—B.M.J. i./o8,942.

* **Antexema Granules.**—Calcium Sulphide 0.06.—L. i./24,256. (As sold in Italy.)

* **Antidipso.**—(Drink cure) Chlorate of Potash and Sugar.—L. ii./o3,1493. White Powders.—Potass. Brom. 24.5, Milk Sugar 75.5%. Coloured Powder.—Potass. Brom. 35, Milk Sugar 65%.—B.M.J. i./o9,910.

* **Anti-fat.**—See Allen's antea.

* **Antipon.**—(Obesity).—Contained 39 grains per ounce of Citric Acid. B.M.J. ii./o7,25.

Anturic Bath Salts.—Analysis showed the salt to consist of Sodium Carbonate (reckoned as Anhydrous) 96.86%, Water 2.70%, Chloride, Potassium salt, perfume, traces.—B.M.J. i./10,393.

Atkinson & Barker's Infants' Preservative.—

Analysis showed in 100 by measure.—Potassium Bicarbonate 1.75, Magnesium Carbonate 5.45, Essential Oil about 0.06, Alcohol 7.0 by measure, Sugar 9.9 colouring matter a trace.—B.M.J. i./12,683.

* **Balsam of Aniseed.**—See Powell's.

* **Beecham's Pills.**—(Aperient) Aloes, Ginger and Soap.—L. ii./o3,1493. Quantities as follows were found:—Aloes 0.5 grain, Powdered Ginger 0.55 grain. Powdered Soap 0.18 grain in a pill.—B.M.J. i./o9,32.

Formula in S.R. is stated to be incorrect,—several important ingredients omitted.—A large proportion of the ingredients come from foreign countries.—Sir Joseph Beecham, Evidence before Proprietary Medicine Enquiry.—P.J. i./13,102, see also Umney, C.D. ii./12,723; C.D. i./13,563.

Sir J. Beecham admitted having altered his formula.—E. F. Harrison, C.D. i./13,650.

* **Beecham's Cough Pills.**—Results of Analysis obtained pointed to the formula: Morphine 0.0035 grain, Powdered Squill 0.1 grain, Powdered Aniseed 0.3 grain, Ammoniacum 0.3 grain Extract of Liquorice 0.4 grain.—B.M.J. ii./o8,1699. The composition has been altered from time to time. Originally they contained some Morphine, then to comply with the Pharmacy Act this was removed. It has been replaced in trivial amount and the pills need not be labelled "Poison."—Sir Joseph Beecham, P.M.C.E., P.J. i./13,102.

Bell-ans (formerly Bell's Pa-pay-ans).—Papain 0.06, Vegetable Charcoal 0.06, Bicarbonate of Soda 0.06, Oil of Peppermint 0.002, Oil of Gaultheria 0.002.—L. i./24,256. (As sold in Italy.)

Bell's* Fairy Cure.—Powders each containing Acetanilide and Phenacetin each 1.16 grains, Caffeine 0.38 grain.—B.M.J. ii./o6,28.

* **Bengue's Balsam.**—Analysis showed the composition to be:—

Menthol 18, Methyl Salicylate 20, Lanolin Anhydrous 54 and a fat, apparently Lard, 8%.—B.M.J. ii./10,986.

* **Bile Beans, Charles Forde's.**—Average weight 2.3 grains. Examination showed Aloin, powdered Cardamoms, Oil of Peppermint, Wheat Flour and possibly presence of Colocynth.—B.M.J. i./11,1326.

Birley's Anticatatrrh.—Analysis showed presence of: Sugar 74, Tartaric Acid 1.15, Phosphoric Acid 0.07, Alcohol trace, Water to 100. No free phosphorus could be detected, but odor suggested a trace.—B.M.J. ii./o2,1286

* **Bismolan for hæmorrhoids.** Bismuth Oxide 0.1, Zinc Oxide 0.15, solution of Suprarenin (1 in 1,000), 0.05, Eucaine Hydrochloride 0.05, Menthol 0.05, Lanolin and Vaseline (equal Parts), 2.—P.J. i./28,349.

* **Bisurolds.**—See International Chem. Co.

* **Blair's Gout Pills.**—Active ingredient is Colchicum.—L. ii./o3,1493. Quantities found indicated Powdered Colchicum Corm. 2.1 grain, Burnt Alum, 0.35 grain in one pill.—B.M.J. ii./o8,1110. (P) According to this Analysis.

Blanchard's Aniol and Steel Pills.—Freed from coating the pills had an average weight of 1.9 grains. Analysis showed presence of Sulphate of Iron, Soap, Barbadoes Aloes, Powdered Ginger, Cardamom, and Cinnamon, also a little Aniol.—B.M.J. ii./11,36.

(P) **Bow's Liniment.** Syn. Anodyne Liniment. Dr. Bow's formula: Hard Soap 4, Opium 8, Ammoniated Camphor Liniment 60, macerate and filter. Dr Bow's modified formula is Ammoniated Camphor Liniment 6, Belladonna Liniment 1, Soap Liniment 6, Strong Ammonia 1, Tincture of Opium 6, Mix, stand 7 days, and filter. These and other formulæ are given.—P.J.F., 1907.

* **Box's Pills (see also Golden Fire).**—Average weight 2½ grains. The following formula gave a pill substantially agreeing in character with the pill

under examination.—Powdered Capsicum 35, Powdered Gentian 15, Flour 15, Aloes 20, Soap 5, Water to 100 parts.—B.M.J. ii./10,087.

Bristol's Pills.—Socotrine Aloes 0·06, Powdered Rhubarb 0·05, Powdered Scammony 0·03, Hard Soap 0·02, Simple Syrup sufficient quantity.—L. i./24, 256. (As sold in Italy.)

(P) ***Bromidia.**—(Neuralgia), Potassium Bromide, Chloral, Hyoscyamus, Cannabis Indica, Aniseed Oil, Syrup and Water.—L. ii./03,1493.

(P) ***Brompton Consumption and Cough Specific.**—The formula is approximately Liquid Extract of Ipecacuanha 0·75, Tincture of Opium 1·3, Treacle 75. Water to 100.—B.M.J. ii./08,506.

Brou Injection, see Injection.

***Brown's Bronchial Troches.**—Chemical analysis and microscopical examination showed the presence of Powdered Cubebs (also possibly Extract) about 6%, Extract of Liquorice in small quantity, Gum and Sugar (about 70%).—B.M.J. ii./11,1543.

***Bunter's Nervine.**—Creosote, Chloroform, Camphor, Balsam of Tolu and Alcohol.—L. ii./03,1493.

***Burgess' Lion Ointment.**—The following is similar—Lead Plaster 13, Beeswax 20, Resin 11, Olive Oil 12, Water 6, Lard to 100.—B.M.J. ii./07,393.

***Burgess' Lion Pills.**—Average weight $4\frac{1}{2}$ grains without coating. Examination indicated Ipecacuanha, Rhubarb, a little Jalap. probably Aloes (Socotrine). Oil of Peppermint and Soap.—B.M.J. i./11,1327.

***Bynin Emulsion of Cod Liver Oil with Hypophosphites.**—Oil 34·6%, Reducing Sugars (as Maltose) 9·0%, Protein 1·2%, Hypophosphite in very small quantity.—B.M.J. i./10,30.

***Bynol.**—Oil 12·9%, Reducing Sugar (as Maltose) 52·2%, Protein 4·6%, Diastatic Power 22.—B.M.J. i./10,30.

***Cadum.**—Analysis showed Zinc Oxide 11·3, Flowers of Sulphur 8·0, Boric Acid 3·1, Salicylic Acid 0·8, Oil of Cade 7, Hard Paraffin 10, Soft Paraffin 60%.—B.M.J. ii./10,1352.

***California Syrup of Figs.**—Senna (active constituent), Syrup of Figs and Cinnamon.—L. ii./03,1493

***Capsuloids.**—Result of analysis indicated for the contents of the Capsules—Hæmoglobin 1·97 grains, Olive Oil and Oleic Acid of each 0·54 grains, Balsam of Peru and Purified Storax 0·17 grain in one Capsule.—B.M.J. i./08,833.

***Carnrick's Liquid Peptonoids.**—100 parts contained Alcohol 20, Total Solids 18·8, Nitrogen 0·8 (equivalent to Protein 5·0), Ash 0·8, Reducing Sugar calculated as Glucose 7·7, Cane Sugar 2·4.—B.M.J. ii./09,562.

Conditions of Sale by Registered Chemists—see Vol. I., p. 664.

***Carter's Little Liver Pills.**

B.M.J. i./11,1326 states—Freed from coating average weight of the pill is $\frac{1}{2}$ grain, evidence of Aloes (Barbadoes) or a preparation of, Podophyllin, Powdered Liquorice Root and Wheat Starch was obtained.

***Cascarets.**—Ext. of Cascara Sagrada ("rendered non-bitter") 0·12, Ext. of Licorice 0·25, Oil of Aniseed, Oil of Peppermint, Powdered Acacia, Sugar sufficient quantity.—L. i./24,256. (As sold in Italy.)

Cassen's (Dr.) Blood Cleansing Tablets.—Weight about 6 grains each. Analysis showed Phenolphthalein 0·75, Pot. Iodide 1·25, Sugar 81, Tale approx. 11, Calcium Carbonate and Sulphate approx. 2, Water 1, Extractive 3%. The dose of Phenolphthalein in one Tablet is 0·045 grain, and the dose of Potassium Iodide is 0·075 grain.—B.M.J. ii./10,1352.

C.B.Q. Post's Tablets we understand are exempt from Poisons' Schedule, 1908. Analysis made in 1908 showed that each tablet contains $1\frac{1}{2}$ grains of Potassium Iodide, a small quantity of Salicylate, a vegetable Extract and Magnesia, also a small quantity of Alkaloid which was not identified.—'Secret Remedies.'

(P) **C.B.Q. Liniment No. 1.** (No. 2 not poison).

***Celmo No. 1.**—The proportions of the various constituents were determined as accurately as practicable, and indicated the following formula—Acetyl-Salicylic Acid 35·5, Powdered Charcoal about 8·0, Malt Extract, dry 18·0, Magnesium Silicate 14·5, other Mineral Constituents 2·8, Water 12·3, Alkaloid 0·5, Extractive about 8·0%. Oleo-resin of Capsicum a trace, Oil of Juniper, a trace.—B.M.J. ii./10,986.

***Celmo No. 2**—An analysis showed these Tablets to contain Pepsin, about 3 grains in each Tablet together with Diastase (probably in the form of Malt Extract) and Socotrine Aloes. No evidence was found of any other ingredient.—B.M.J. i./12,438.

Chameleon Oil.—A mixture prepared by the following formula agreed in physical and chemical properties with the original, except in regard to some minor characters of the Resins. Essential Oils of Mustard 0.75, Spearmint 0.45, Pimento 1.5, Cassia 1.5, and Camphor 13.0, Oil of Turpentine 15.0, Alcohol (90%) 7.3, Strong Solution of Ammonia 8.0, Resins 1.6, and Water to 100. All in parts by measure.—*B.M.J.* ii./10,983.

Ⓟ ***Chlorodyne, Dr. J. Collis Browne's.**—(Coughs, etc.) Chloroform, Ether, Morphine, Cannabis Indica, Capsicum, Peppermint and Treacle.—*L.* ii./03,1493; ii./06,1390. Does not now contain Hydrocyanic Acid. Further it contains less than 0.2% Morphine (Anhydrous).

Cicfa.—See "Mother's Advice."

***Clarke's Blood Mixture.**—Potassium Iodide 52.5 grains, Spirit of Sal Volatile 10 minims, Spirit of Chloroform 67 minims, Simple Syrup 50 minims, Burnt Sugar q.s., Water to 8 ounces.—*L.* ii./03,1493. *B.M.J.* ii./07,530. Contains no Sal Volatile but an entirely different preparation of Ammonia.—*E. J. Parry, P.M.C.E., C.D.* i./13,562. *E. F. Harrison's reply, C.D.* i./13,651.

***Cockle's (James) Pills.**—Average weight 4 grains. Analysis indicated presence of Aloes, a little Soap, Powdered Colocynth, Powdered Jalap, and another vegetable tissue which could not be identified.—*B.M.J.* i./11,1327.

***Coleman's Wincarnis.**—Wineglassful (2 ounces) would contain Alcohol 3 drachms, 8 minims, Meat Extract 10.5 grains, Glucose 159 grains.—*B.M.J.* i./09,795. See also Manufacturers in answer to Dr. Mary Sturge.—*B.M.J.* i./13,724.

***Congreve's Elixir.**—(Cough Mixture).—*L.* ii./03,1493. Analysis of the Elixir showed 28.5% by volume of Alcohol together with resinous material similar to the resins of Benzoin, Storax, Tolu or Balsam of Peru, Sugar about 1%. Alkaloid under 0.001%.—*B.M.J.* ii./08,505.

Carton round the bottle states 'no poison whatever' and this we have reason ourselves to believe.

***Crosby's Balsamic Cough Elixir.**—Contains inter alia Invert Sugar 58%, Alcohol 10.6%, Acetic Acid 0.3%, see *B.M.J.* (ref.) Sulphuric Acid corresponding to 44 minims of the official dilute Sulphuric Acid in one ounce.—*B.M.J.* ii./08,1699.

Curic Wafers.—Acetanilide 3.28 grains, Phenacetin 3.28 grains, Caffeine Citrate 1.64 grains each.—*B.M.J.* ii./06,27.

***Curicones.**—Analysis showed Sulphur, Lactose, Guaiacum Resin (about 10%), Acetyl-Salicylic Acid, Sodium Benzoate (about 25%), and a powdered vegetable drug resembling Cimicifuga Rhizome. Average weight of contents of one capsule is about 2½ grains.—*B.M.J.* i./15,992.

***Cuticura.**—Hard and Soft Paraffins, slightly perfumed with rose and coloured green.—*B.M.J.* i./08,943.

***Cuticura Pills.**—Aloin 0.02, Jalapin 0.02, Podophyllin 0.008, Capsicin 0.001.—*L.* i./24,256. (As sold in Italy.)

***Cuticura Resolvent.**—Potassium Iodide, Sugar and Glucose, Extractive, Alcohol and Water.—*B.M.J.* i./08,944.

***'Daisy' Powders** consist of Acetanilide alone, hence exempt from Medicine Stamp Duty. Each powder contains 5 grains.—*B.M.J.* ii./06,27; *L.* ii./06,1390; *C.D.* i./13,529.

Dixon stated before the Proprietary Medicine Committee that Acetanilide is a dangerous drug, and that "lots of deaths" had been caused by headache powders containing it. J. Lawson representing "Daisy" however, pointed out that this is not supported by the Registrar General's returns for the last ten years, only one death being recorded as caused by headache powders (phenacetin), namely in 1908.

Statements have been made that there have been numerous deaths in America from use of Acetanilide. "Daisy" is not intended for Children.—*C.D.* i./13,529; *P.J.* i./13,472.

NOTE.—* "BUTTERCUP" is a trade mark of "Daisy, Ltd." Details of the introduction of the Company's "Head Powder."—*C.D.* i./13,529. These consist of Phenacetin alone. Vide Head Powders.

Dalby's Carminative.—Rhubarb, Magnes. Carb., Glycerin, Sugar, Peppermint Oil, Dill Oil, and a small quantity of Laudanum.—*L.* ii./03,1493. Proprietors say not a poison.

***Damaroids.**—Freed from coating the Tablets had an average weight of 3.9 grains. The figures arrived at were Iron Hypophosphite 14.2, Quinine Sulphate 3.4, Extract (probably Damiana) 50, Sugar, Talc 16%.—*B.M.J.* i./11,27

Darley's Toothache Plasters (JOHNSON & JOHNSON).—Pimento, Black Pepper, Cloves, 10 per cent. of each, Rubber solution sufficient quantity.—*L. i./24,256. (As sold in Italy.)*

* **Davis' Famous Female Pills**.—*Inter alia*, Powdered Savin $1\frac{1}{2}$ grain in each with Sulphate of Iron.—*B.M.J. ii./07,1654. Proprietary say not a poison. A mixture made by them contains Gossypium.—ibid.*

* **"D.D.D."** (For eczema). Analysis showed Salicylic Acid 0.75, Phenol 1.18, Methyl Salicylate (Oil of Wintergreen) 1.00, Glycerin 9.28, Alcohol 65.10, by measure, Water to 100 parts by measure.—*B.M.J. ii./10,1350.*

De Roos' (Dr.) Compound Renal Pills.—Freed from coating average weight of pills was 4.5 grains.—Contained Soap 34.2, Sodium Carbonate 19.7, a Resin (uncertain, probably Ammoniacum) 3.3, and a small quantity of vegetable tissue with moisture and extractive. Vegetable tissue could not be identified.—*B.M.J. ii./11,78.*

Dearborn Ltd's. Preparations.—'Stallax' and 'Allacite of Orange' before the P.M.C.E.—*P.J. i./13,770; C.D. i./13,831; B.C.D. i./13,506.*

Dixon's Pills.—(Aperient. Liver) Taraxacum, Podophyllin, Jalap and Soap.—*L. ii./03,1493.*

* **Doan's (Backache Kidney) Pills**.—1. White-coated aperient Dinner Pills—Podophyllin, Aloin, Rhubarb and Peppermint 2. Brown-coated (Backache) Pills—Oil of Juniper and a resinous constituent (? Benzoin). *L. ii./03,1493. B.M.J. ii./06,1646 gives as similar to the Dinner Pills a pill composed of Podophyllin, Aloin, Peppermint Oil, Jalap, Capsicum and Henbane Extract (this formulæ would of course be (P)): and for the Backache Pills, Juniper Oil, Hemlock, Pitch, Potassium Nitrate and Fœnugreek—in both instances with excipients in addition.—Parry has also reported on harmlessness of.*

* **Doan's Dinner Pills**.—There is at any rate one most important constituent omitted from above analysis.—Umney, P.M.C.F., C.D. ii./12,721.

* **Doan's Ointment** (for piles) Calomel 36.6, Zinc Oxide 11.2, Phenol 1.3, Beeswax 2.3, Soft Paraffin 49.2%.—*B.M.J. ii./08,87.*

Dodd's Kidney Pills.—A Pill containing Cascarella, Jalap, Soap, Potassium Nitrate, Sodium Bicarbonate, Hard Paraffin, Turmeric and Wheat Flour is stated to be practically identical.—*B.M.J. ii./06,1646.*

Dusart's Wine.—Alcohol 16.85, Glucose 12.8, Iron 0.09, Calcium 0.07, Phosphorus calculated as Phosphoric Acid 0.03%.—*B.M.J. i./09,1309.*

* **Dyxol**.—A mixture prepared in accordance with the following formula was practically indistinguishable from the original:—Essential Oils of Mustard 20, Nutmeg 20 and Allspice 4, Cottonseed Oil 6, Liquid Paraffin (yellow) 17, and Kerosene 33%—all by volume.—*B.M.J. ii./10,984.*

* **(P) Eade's Gout and Rheumatic Pills**.—The formula was found to be Barbadoes Aloes 10, Colchicum Extract 18, Colchicum Corm. powdered 35, Treacle 27, Gum and Dextrin 10%.—*B.M.J. ii./10,982. Must be labelled with word Poison and name and address of seller.*

Eau de Blanc de Perles.—Contains *inter alia* about 15% Lead Carbonate.—*Murrell.*

(P) Eau de Fleurs de Lys contains a trace of Corrosive Sublimato.—*Murrell.*

Ecorces d'arémone.—Soft Soap 75, Glycerin 25, Potassium Iodide 15, Borax 1, Citral 2, Distilled Water 88.—*L. i./24,256. (As sold in Italy.)*

* **Eczoline Ointment**.—Analysis showed Flowers of Sulphur 39, Zinc Oxide 3.7, Glycerin 13.5, Lard 39.8, Water 4%, Oil of Lemon a trace.—*B.M.J. ii./10,1351.*

* **Eczoline Tablets**.—Analysis showed Ferrous Sulphate 16.5, Sulphur (precipitated) 56, Talc 3.4, Starch 7.3, Extractive 16.8. The Extractive appears to be a mixture of Cascara Sagrada and an inert Extract,—the former constituting about 5% of the substance of the Tablets.—*B.M.J. ii./10,1351.*

* **Elliman's Embrocation**.—Acetic Acid (30 per cent.) 180, Oil of Turpentine 300, Camphor 20, Egg Yolk 100, Distilled Water 400.—*L. i./24,256. (As sold in Italy.)*

* **Euo's Fruit Salt**.—(Aperient) Sodium Bicarbonate, Tartaric Acid and Citric Acid.—*L. ii./03,1493. Contains no Sodium or Magnesium Sulphate. Eucol.—B.M.J. i./10,762.*

* **Evans's Antiseptic Throat Pastilles**.—(Special Formula for Italy).—Essential Oil of Pine 0.01, Menthol 0.002, Chlorate of Potash 0.003, Borax 0.03, Ext. of Licorice 0.07, Powdered Acacia, Sugar sufficient quantity.—*L. i./24,256.*

(P) ***Fellow's Compound Syrup** (of) Hypophosphites contains poison.—*L. ii./05,1390—vide also Vol. I., p. 692.*

***Fenning's Children's Cooling Powders.**—Average weight 3.4 grains. Analysis showed powder to consist of Potassium Chlorate 70, Powdered Liquorice 30%.—*B.M.J. ii./08,1022.*

***Fenning's Lung Healers.**—Average weight of one pill was 0.22 grains, chemical analysis and microscopical examination showed presence of Ipecacuanha only. Alkaloid present amounted to 1.8%.—*B.M.J. ii./11,1543.*

***Figuroids.**—The large tablets contained by analysis Sodium Bicarbonate 38.9, Tartaric Acid 13.1, Sodium Chloride 3.8, Phenolphthalein 1.2, Formamine (Hexamethylenetetramine) 2.0 grains. The small Tablets 11.9, 15.9, 7.6, 0.5 grains respectively of the first four.—*B.M.J. ii./08,1567; i./09,556.*

Forde's (Chas.) Bile Beans, see Bile Beans.

Fosfiron.—Iron Nucleophosphate 0.06, Calcium Glycerophosphate 0.3, Cinchona Alkaloids 0.05, Caffein 0.03.—*L. i./24,256. (As sold in Italy.)*

Foster's Backache and Kidney Pills.—Potassium Nitrate 0.024, Ginep (? Juniper) 0.005, Uva Ursi 0.008, Venice Turpentine 0.024, Excipient sufficient quantity.—*L. i./24,256. (As sold in Italy.)*

*** (P) Foster's Digestive Pills.**—Podophyllin 0.011, Leptandrin, Ext. of Hyoscyamus, Aloin, of each 0.008, Rad. (?) Jalap. 0.004. "With tonics and laxatives."—*L. i./24,256. (As sold in Italy.)*

(P) Freeman's Chlorodyne contains less than 0.2% Morphine and does not contain Prussic Acid.—*By the Makers.*

Fucol is Sesame Oil containing a small quantity of Iodine. It is said to be made from Seaneed.—*B.M.J. i./07,879.*

Gautier's Female Pills.—Freed from coating the pills had an average weight of 3.8 grains. Analysis showed a small quantity of Aromatic Essential Oils (Pennyroyal, Rue and possibly Tansy) and probably Apiol. Principal constituents were Exsiccated Sulphate of Iron 10% and Soap 11%, Powdered Liquorice 30%, a little Powdered Ginger, and a small quantity of apparently Socotrine Aloes.—*B.M.J. ii./11,35.*

(P) Gelineau's Dragees for Epilepsy are stated to contain Potassium Bromide, 1 in 1,000 Antimony Arsenate and 1 in 2,000 Picrotoxin. (Might be viewed as (P).)

Genoform.—Formula of the Tablets is Salicyl-Methylene-Glycol-Ester 95, Starch and moisture 5%.—*B.M.J. ii./08,1113.*

Glant Remedy, The—see Box's Pills and Golden Fire.

Glendenning's Beevinalt (Beef and Malt Wine).—Wineglass (2 ounces) contains Alcohol 3.33 drachms, Meat Extract 3.5 grains, Glucose 93 grains.—*B.M.J. i./09,796.*

*** Gloria Tonic.**—(Gout and Rheumatism) Tablets. The following formula was indicated: Potassium Iodide 1.8, Guaiacum Resin 0.8, Ext. Liquorice 1.0, Resinoid (Phytolaccin?) 0.9, Powdered Liquorice 1.7, Rice Starch 2.0, Talc and Kaolin 2.1 grains. *** Gloria Pills.**—The following was indicated: Extract of Cascara 0.3, Ext. Soc. Aloes 0.5, Jalap Resin 0.07 grain, Flour and excipient q.s. in one pill.—*B.M.J. ii./08,1111; see also L. ii./03,1493.*

Glykaline.—(For coughs, colds, catarrhs, etc.) Analysis showed the liquid to contain 35% of Alcohol and 0.15% of solid matter consisting of Potassium Iodide and partly of organic matter. Each dose would contain $\frac{3}{16}$ grain of Potassium Iodide, with a trace of organic matter which may be derived from some drug.—*B.M.J. ii./11,1544*

*** Golden Fire.**—The following is the formula given by the analyst:—Oil of Amber 0.16, Oil of Rosemary 0.16, Oil of Eucalyptus 0.32, Oil of Camphor essential 1.3, Sodium Chloride 6.4, Glacial Acetic Acid 6.4, Alcohol 1.0 and races of decoction of Capsicum. Barley and Lobelia.—*B.M.J. ii./10,987.*

Guy's Tonic.—Phosphoric Acid, Tinct. Cochineal, Inf. Gentian and Chloroform Water.—*L. i./03,1493. B.M.J. i./11,26* gives the following formula as an exactly similar mixture.—Dilute Hydrochloric Acid 0.59, Dilute Phosphoric Acid 0.52, Alcohol 2.27, Compound infusion of Gentian 40, Chloroform Water 50, Cochineal q.s. Water to 100 parts by measure.

*** Hair's (Dr.) Cure for Asthma.**—A fluid containing 5.6% Potassium Iodide, Tar Water and some Wine.—*L. ii./03,1493; B.M.J. i./07,879.*

*** Hall's Wine.**—Previously contained Cocaine, but contains none now.

Hardy's Cough Specific see Brompton Consumption and Cough Specific.

Harvey's Blood Pills.—Contain among other ingredients about $\frac{1}{2}$ grain.

each Quinine Sulphate, about $\frac{3}{4}$ grain Potassium Iodide and about $\frac{1}{2}$ grain Rhubarb.—*B.M.J.* ii./07,530.

Head Powders prepared by Daisy Ltd., consist of Phenacetin alone—8 grains in each.—*J. Lawson, C.D.* i./13,530. cf. *Daisy Powders*.

Headache Powders usually contain Acetanilide, 3 grains each.

Hoffman's (Dr.) Rheumatic Powders :—

Analysis showed the following composition,—Acetyl-Salicylic Acid 66.4, Phenacetin 11.4, Caffeine 1.3, Sugar 20.1, Moisture 0.8%.—*B.M.J.* ii./10,982.

***Holloway's Ointment**.—Fresh Butter, Beeswax, Yellow Resin, Vinegar of Cantharides, Canada Balsam, Expressed Oil of Mace, Balsam of Peru or Liquid Storax.—*Murrell*.

We understand, however, from the makers that this contains nothing of a poisonous nature, and is not (P).

***Holloway's Pills**.—*B.M.J.* i./11,1326 states "The Pills had an average weight of 1.4 grains, examination showed the presence of Aloes (Barbadoes) or a preparation of Aloes, Powdered Ginger and Soap."

Holroyd's Gravel Pills.—Average weight of Pill freed from coating was 4.3 grains. From analysis the following formula was arrived at—Soap 40, Dried Sodium Carbonate 20, Powdered Rhubarb 20, Oil of Anise 10, Syrup 10.—*B.M.J.* ii./11,77

Hood's Sarsaparilla.—Dose $\frac{1}{2}$ to 2 teaspoonfuls. Analysis indicated 19% by volume of Alcohol and $7\frac{1}{2}$ grains of Potassium Iodide in the ounce, the amount of Sarsaparilla being small.—*B.M.J.* ii./07,531.

Hood's Vegetable Pills.—After removal of coating average weight was $\frac{1}{2}$ grain. Examination showed Aloes (Barbadoes) or a preparation of Aloes—probably Aloin, Ginger, Capsicum, Colocynth, Soap and probably a little Jalap.—*B.M.J.* i./11,1327.

Hooper's, Dr. John, Female Pills.—Analysis showed Iron Sulphate, Aloes, Jalap, Canela, Senna and Oil of Pennyroyal.—*B.M.J.* ii./07,1653.

***Horton's Benedict Pills**.—Average weight 4 grains. Analysis showed Sulphate of Iron corresponding to 10% Exsiccated Sulphate, Socotrine Aloes Powdered Ginger and a vegetable powder probably Gentian.—*B.M.J.* ii./11,36.

***Hughes' Blood Pills**.—Contain Aloes, Jalap, &c.—*B.M.J.* ii./07,532.

Hyomee**. (Hyomei** is T.M.)—From examination it was concluded that Alcohol and Liquid Paraffin formed each about 10% of the whole, Eucalyptus Oil (and possibly other Oils) appears to form the remaining 80%,—a small proportion of a mixture containing Wood Tar and Creosote was also indicated.—*B.M.J.* ii./11,1544.

Indian Tincture.—Capsicum, Cannabis Indica, Ether and Methylated Spirit.—*Murrell*.

(P)**Injectio *Brou**.—Zinc Sulphate, Sugar of Lead, Laudanum, Tinct. Catechu and Water.—*Murrell*. Pharm. Form. says:—Zinc Sulphate 15 grains, Lead Acetate 30 grains, Catechu Tincture 1 drachm, Tinct. Opii Crocat (q.v.) 1 drachm, Water to 6 ounces. is generally adopted in making imitations.

International Chemical Co's *Bisuroids.—Each tablet contains Phenolphthalein 0.135.—*L.* i./24,256. (As sold in Italy.)

Invigoroids.—The formula arrived at was:—In one Tablet, Ext. Nucis Vom. 0.028 grain, Zinc Phosphide 0.067 grain (calculated from Zinc present). Saccharated Carbonate of Iron 0.50 grain, Asafoetida 0.25 grain with some Sugar of Milk.—*B.M.J.* i./11,91. This may be (P).

***Iodia, Battle**.—Liq. Ext. of Queen's Root, False Unicorn Root, Pimpinella, Saxifrage, Menispermum, equal parts to 125, Pot. Iodide 7.5, Iron Pyrophosphate 5.—*L.* i./24,256. (As sold in Italy.)

I.R.S. Compound Golden Tablets.—Contain Ferrous Sulphate and Sodium Carbonate.—*B.M.J.* ii./07,1658.

James' Fever Powder.—Antimonious Oxide 1, Calcium Phosphate 2.

***Johnson's (Mrs.) American Soothing Syrup**.—Analysis showed in 100 by measure Sodium Chloride 5.66, Hydrochloric acid (B.P.) 2.33 by measure, Reducing Sugars, calculated as Glucose 66.6, extractive coloring matter etc. about 5.0. The reducing Sugars appeared to be present in the form of Honey, representing about 85 parts of this.—*B.M.J.* i./12,683.

The proprietors point out that the preparation does not contain Hydrochloric Acid ("Secret Remedies" and *B.M.J.* state as above), but a third of it is lemon juice. Discussion in the P.M.C.E., C.D. ii./12,23; see also Parry, C.D. i./13, 563.

***Kaputine** (for Headache and Neuralgia).—Contains Antifebrin 6.3 grains

in each, with Sugar 0·21 grains, and coloured with Ferric Oxide 0·05 grain.—*L. ii./103,1493 B.M.J. ii./106,28.*

Kassium Extract.—*Ext. "cassium lign."* 0·02, *Rad. gossyp. barb.* 0·04, Calcium Glycerophosphate 0·15, Iron Glycerophosphate 0·03, Oil of Aniseed 0·0006; Excipient sufficient quantity.—*L. i./24,256. (As sold in Italy.)*

***Karo Compound.**—The contents of several bottles of this preparation were examined and were found to differ very considerably in composition. Magnesium Sulphate varied from 1·45 to 6·87%. Potassium Citrate from 4·76 to 6·55%, Sugars about 8%. The Alcohol in one specimen was 6%, Nitrous Ether was present and a trace of Nitrite, Vegetable Extractive was between 1 and 2% but showed no characters indicative of its source. Microscopical examination of the sediment showed the presence of yeast-like cells and the minute plants known as desmids.—*B.M.J. ii./11,79.*

(P)*Kay's Linseed Compound.

100 parts contained 1·07 parts of Chloroform, and 4·3 parts of Alcohol both by measure, 67 parts of Solids—about 48 parts of the latter sugar, and the remaining 19 parts consisted principally of the mucilage of decoction of linseed. Ipecacuanha alkaloids extracted amounted to 0·007%, and the Morphine to 0·021%.—*B.M.J. ii./108,1698.*

There is in the S.R. Analysis no mention of Senega which is one of the principal ingredients, while the analysis states that Ipecacuanha is present but there is no mention of it on the label.—*Umney, P.M.C.E., C.D. ii./12,891.*

***Kay's Tic Pills.**—Iron Sulphate, Quinine and Soap.—*L. ii./103,1493.*

(P)*Keating's Pectoral Lozenges.—Corresponded to Morphine 0·007 grain, Ipecacuanha 0·07 grain, Extract of Liquorice 2·1 grain, Sugar 13 grains in one lozenge.—*B.M.J. ii./108,1699.*

***Keene's "One Night" Cold Cure.**—Ingredients found were Cinchonidine Sulphate 0·21 grain, Acetanilide 0·32 grain, Calcium Carbonate 0·25 grain, Starch 0·34 grain, Extractive and excipient 0·87 grain (all figures approximate).—*B.M.J. ii./108,1286.*

***Kepler Solution of Cod Liver Oil in Malt Extract.**—Analysis showed Oil 17·4%, Reducible Sugar (as Maltose) 42·5, Protein 3·4, Diastatic Power 3.—*B.M.J. i./10,30.*

***Ker-nak Pills.**—Average weight without coating $1\frac{1}{2}$ grain. Examination indicated Aloes, a little Soap, a very little Oleo-resin of Capsicum, and a little vegetable tissue resembling Marshmallow root.—*B.M.J. i./11,1327.*

***Kilmer's (Dr.) Indian Cough Cure.**—Contains *inter alia* (see ref.) 0·5% Oil of Pumilio Pine. No alkaloid.—*B.M.J. ii./108,1698.*

***Koko.**—Borax 1·4, Glycerin 1·7, Formaldehyde Solution (40%) 0·1, Perfume a trace, Alcohol 3, Water to 100 by volume.—*B.M.J. i./10,151.*

***Kolynos Dental Cream.**—Calcium Carbonate 21, Soap 25·5, Thymol 0·25, Benzoic Acid 0·3, Sarcharin 0·5, Eucalyptus Oil 1·75, Peppermint Oil 1·9, Glycerin 27, S.V.R. 21·8.—*Stated by the Makers.*

***Lactopeptine Powder.**—Lactose 40 oz., Pepsin 8 oz., Pancreatin 6 oz., Diastase 4 drachms, Lactic Acid, Hydrochloric Acid, of each 5 fl. oz.—*L. i./24,256. (As sold in Italy.)*

Lady Webster's Pills.—Aloes 2 grains, Powdered Mastiche $\frac{1}{2}$ grain, Red Rose Leaves $\frac{1}{2}$ grain with Syrup of Wormwood.—*Murrell.*

***Lamplough's Pyretic Saline (Aperient).**—Citric Acid, Potassium and Sodium Bicarbonates.—*L. ii./103,1493.*

Lane's (Dr.) Catarrh Cure.—Analysis showed Phenol 0·4, Sodium Chloride 3·3, Water to 100.—*B.M.J. ii./108,1285.*

Langdale's Cinnamon Tablets.—Oil of Cinnamon 0·25, Powdered Acacia, Sugar sufficient quantity. Coloured with Carmine.—*L. i./24,256. (As sold in Italy.)*

Langdale's Essence of Cinnamon.—Oil of Cinnamon 0·30, Tinct. of Cinnamon 30, Alcohol (90 per cent.) 54.—*L. i./24,256. (As sold in Italy.)*

*** (P)Laville's Gout Cure.** Colchicine about 0·08% and Quinine in Alcoholic Solution.—*B.M.J. ii./107,677.*

The following is similar, (Ph. Form.)—Quinine 4 drachms, Colocynth Extract 2 drachms, Alcohol 90% 4 ounces, Malaga Wine 15 ounces. Mix and filter. Dose.— $\frac{1}{2}$ to 4 drachms in $\frac{1}{2}$ wineglass of water.

The Pills are (Ph. Form.) Extract of Winter Cherry 3 dr., Sodium Silicate 1 dr. Make a mass and divide into 5 grain Pills. Dose.—4 to 10 daily. Guaiacum Resin a constituent with the Silicate and Winter Cherry and other ingredients.—*Vide Secret Remedies.*

★ **Lemco Meat Wine.**—A wineglassful (2 ounces) would contain Alcohol 2.75 drachms, Meat Extract 5.2 grains, Glucose 112 grains.—*B.M.J.* i./09,795.

★ **Licoricine.**—Does not contain poison.—*L.* ii./06,1390.

★ **Liebig's Meat and Malt Wine.**—See *Lemco*.

★ **Lilly's (Nurse) Female Pills.**—Freed from coating, average weight was 1.9 grains. Contain Sulphate of Iron, 12%, Socotrine Aloes, Cinchonine Sulphate 3.3%, Powdered Capsicum about 30%, a little Powdered Ginger and Pennyroyal.—*B.M.J.* ii./11,36.

★ **Liquifruta (A Consumption Cure).**—Analysis showed Oil Peppermint, Onion or Garlic Oil and Alkaloids, of each traces, Potassium Bitartrate 0.4, Glucose 34.4, Cane Sugar 2.28, Mucilage, Tannin, Extractive, etc. and water to 100.—*B.M.J.* ii./09,1419.

★ **Lockyer's Sulphur Hair Restorer.**—Precipitated Sulphur 1.3%, Lead Acetate 1.6, Lead Sulphate 0.4%, Glycerin 9.6%, Rose Water to 100 by volume.—*B.M.J.* i./10,151.

★ **Locock's Pulmonic Wafers.**—*Lactucarium*, *Ipecacuanha* and *Squills*.—*Murrell*. This form would make the preparation (P).

★ **McKenzie's (Dr.) "One Day" Cold Cure.**—Analysis showed the Tablets to have composition Cinchonidine Sulphate 0.83 grain, Acetanilide 0.71 grain, Camphor 0.1 grain, Tale 0.21 grain, Water 0.15 grain.—*B.M.J.* ii./08,1285.

★ **Mariani Wine.**—Alcohol 36.3, Total Solids 30.3, Ash 0.2. Reducing Sugar (as Glucose) 9.8, Cane Sugar 17.5, Alkaloids 0.025.—*B.M.J.* ii./09,562.

★ **Marmola.**—Quantitative determination difficult.

Formula arrived at was—Dried Thyroid Gland 1.4 grain, Phenolphthalein 0.4 grain, Sodium Chloride 0.7 grain, Powdered *Fucus Vesiculosus* 5 grains, Extractive 2.5 grains, Oil of Peppermint trace.—*B.M.J.* ii./08,1566. Another analysis. *L.* ii./08,104

★ **Marshall's Cigarettes.**—*Lobelia inflata* 20, *Datura stramonium* 55, *Cubeb* Fruit 20, Potassium Nitrate.—*L.* i./24,256. (As sold in Italy.)

★ **Martin's Apio and Steel Pills.**— $1\frac{1}{2}$ grains of Aloes in each with, inter alia, reduced Iron and Apio each $\frac{1}{10}$ grain.—*B.M.J.* ii./07,1655.

★ **Marza Wine** contains Iron, Phosphorus, Coca and Pepsin. Discussion as to quantities.—*P.M.C.E.*, *C.D.* ii./12,892.

★ **Menstruation Powders.**—Particulars are given of several consisting of Chamomile only.—*B.M.J.* i./10,1189

★ **Mexican Hair Renewer.**—Precipitated Sulphur 1.4%, Lead Acetate 0.1 (one sample examined contained 0.97%), Glycerin 19.0%, Rose Water to 100 by volume.—*B.M.J.* i./10,512.

★ **Miol.**—Analysis showed it to contain Oil 22.4%, Reducing Sugars (as Maltose) 41.3%, Diastatic power 2.—*B.M.J.* i./10,30.

★ **Morison's Pills.**—(For Obesity). Aloes, Jalap Resin, Extract of *Colocynth*, Gamboge, Rhubarb, a.a. 1 Gm. and Myrrh 2 Gm. to make 50 pills. Historical note.—*P.J.* ii./22,381. See also our last Edn., Vol. II. p. 574.

★ **Mothersill's Seasick Remedy.**—Contents of Capsules—a pink and a brown powder on analysis gave the following:—

Pink Powder.—Sugar of Milk 33.3, Caffeine 8.2, Stearic Acid 18.0, Chlorbutol 40.1%, colouring matter a trace.

Brown Powder.—Powdered Cinnamon 29.4, Caffeine 8.4, Stearic Acid 17.4, Chlorbutol 44.5%. Stearic Acid is probably added as a lubricant to assist in filling the capsules though the amount is large for the purpose.—*B.M.J.* ii./10,1928.

★ **Mother's Advice.**—Recently 'Tablenes' and formerly 'Ciefa' and before that 'Tablones.' Contained Pepsin, Diastase and other ingredients.—*B.M.J.* i./09,556.

B.M.J. i./11,1325, gives the following:—Analysis showed presence of Pepsin corresponding to $\frac{1}{2}$ grain Pepsin B.P., diastase, reducing sugar (apparently Maltose), a bitter extract agreeing in characters with Ext. *Cascara Sagrada* about $\frac{1}{2}$ grain, a pungent substance which appeared to be Oleo-resin of *Capsicum* about $\frac{1}{100}$ grain, Tale and a little starch probably derived from the coating.

The starch is not converted by Diastase as inferred in *S.R.*—*E. J. Parry*, *P.M.C.E.*, *C.D.* i./13,563.

★ **Mother Seigel's Syrup.** See *Seigel*.

★ **Munyon's Blood Cure and Munyon's Kidney Cure.**—Granules, entirely Sugar (quantitative determination showed just 100%).—*B.M.J.* i./07,213; ii./07,531.

*Munyon's Catarrh Tablets.—Analysis showed Sodium Bicarbonate 1.87 grains, Sodium Chloride 1.81 grains, Borax, partly dehydrated 2.2 grains Phenol traces, Gum 0.12 grain.—*Secret Remedies*.—B.M.J. ii./08,1286.

*Munyon's Special Catarrh Cure.—Determination showed these pilules to consist of 100% sugar.—B.M.J. ii./08,1286.

*Munyon's Pile Ointment consists of Soft Paraffin with trace of Ichthyl, probably less than 0.2%.—B.M.J. ii./08,87.

*Murray's Fluid Magnesia was run by a medical man, physician to the Lord Lieutenant of Ireland, 1859. Advertised in the first number of "*Chemist and Druggist*."—E. J. Parry, P.M.C.E., C.D. i./13,560; B.M.J. i./13,834.

Naldire's Worm Powders.—Powdered Areca Nut 4, Powdered Jalap 0.5, Powdered Rosemary 0.5.—L. i./24,256. (As sold in Italy.)

*Nervettes, Coleman's.—Phosphorus 0.005 grain and Quinine Sulphate 0.07 grain with vegetable matter 0.3 grain were determined.—B.M.J. i./09,32.

[P] Neuraine.—Aconite, Chloroform and Rose Water.—Murrell (11th Edn.) New Skin.—Pyroxylin 5, Acetone 50, Benzol 20, Amyl Acetate 25.—L. i./24,256. (As sold in Italy.)

*Norton's Chamomile Pills.—Aloes, Gentian and Chamomile Oil.—Murrell.

According to L. i./24,256:—Cape Aloes 0.03, Ext. of Gentian 0.12, Oil of Chamomile 0.02, Powdered Gentian sufficient quantity. (As sold in Italy.)

*Nurse Lilly's see Lilly's.

*Ovaltine.—Described as 'composed of Malt Extract, Fresh Swiss Cow's Milk, Fresh Eggs, and converted Cocoa, and containing active Lecithin.' Analysis showed Fat 12.3%, Reducing Sugars (as Maltose) 60.0%, Nitrogenous substances calculated as Protein 13.4%, Ash 3.5%, Water 1.5%.—B.M.J. i./10,30

*Owbridge's Lung Tonic.—Balsam of Tolu, Oil of Aniseed and Oil of Cloves.—L. ii./03,1493. Does not contain poison.—L. ii./06,1390.

The alkaloids of Ipecacuanha were found to the amount of 0.002%. If present in the form of Winc of the official strength this represents Ipecacuanha Wine 15 m., Chloroform 2 m. in each ounce.—B.M.J. ii./08,1698.

*Oxien.—Powdered Sugar, Starch and Gaultheria Oil.—L. ii./03,1493.

*Oxien Medi-Cone Pile Treatment.—The suppositories weigh on average 19 grains. Analysis showed Lead Acetate 5.6, Creosote about 2, Resinoid substance 3 (showing presence of Tannin), vegetable tissue 1, Hard Paraffin 7, Theobroma Oil 81.4%.—B.M.J. ii./08,87.

*Ozerine (in epilepsy).—Potassium Bromide, Ammonium Iodide with Chloroform Water.—L. ii./03,1493; B.M.J. ii./04,1586, gives approximately Potassium Bromide 120 grains, Ammonium Carbonate 16 grains per ounce (without Iodide), with Chloroform Water, &c.

Page-Woodcock's see Woodcock's.

*Panopepton.—100 contained Alcohol 20, Total Solids 26.9, Nitrogen 1.14 (equivalent to Protein 7.2), Ash 1.1, Sugar 7.8.—B.M.J. ii./09,562.

May be dispensed by registered chemists under certain conditions. Vol. I., p. 662.

Parr's Life Pills.—Aloes, Rhubarb, Jalap, Gentian, Clove Oil.—Murrell.

*Pazo Ointment.—Zinc Oxide 10, Camphor 5, Carbolic Acid 1, Balsam of Peru 4, Ext. of Hamamelidis 6, Yellow Beeswax 4, Benzoated Lard 70.—L. i./24,256. (As sold in Italy.)

*Peps.—B.M.J. ii./11,1543, summarises results of analysis (q.v. for further details), thus: Sugar about 70%, Extract of Liquorice about 25%, Resinous matter 0.7%, Oil of Peppermint a trace, Oil of Anise a trace, Talc about 4%.

*Perry-Davis' Pain Killer.—Spirit of Camphor, Tincture of Capsicum, Tincture of Murrah and Alcohol.—Murrell

*Phyllosan. (T.M. 409946). According to the makers, Phyllosan is a pure form of Chlorophyll. It is made in 2½ grain Tablets.—Y.B.P. '25/200. According to B.M.J. i./22,317, the Tablets contain 0.03 Gm. Chlorophyll and 0.005 Gm. of iron. For the treatment of anaemia, chlorosis and wasting diseases.

Chlorophyll contains no iron in itself but bears some close relation to iron, for it cannot be formed in a plant from which iron is excluded. It contains Magnesium, and perhaps this supplies to the component parts of Chlorophyll the same cement which iron is said to give to the haemoglobin molecule. Phylloporphyrin $C_{16}H_{18}N_2O$, one of the decomposition products of Chlorophyll, has a close relationship to Haematoporphyrin $C_{16}H_{18}N_2O_8$, an iron-free decomposition product of

Hæmoglobin. Going a stage further, Hæmopyrrol $C_8H_{13}N$ can be obtained from both. Bürgi claims that Chlorophyll may be used to aid Hæmoglobin production in the body. It is shown that we get better results from our iron pill and fresh vegetables than from Hæmoglobin preparations. In only one vegetable is Chlorophyll available in large quantities, namely spinach, and even in this it is thought to be so held up in the plant as to be not readily available for man.—*L. i./22,23,90.*

* **Phosferine.**—A weak solution of Quinine in Phosphoric Acid.—*Lancet Supp. on the Sale of Patent Medicines, Jan. 10, 1925,12.*

* **Pink Pills.**—Iron Sulphate, an alkaline carbonate, and Liquorice thickly coated with sugar and coloured with carmine.—*L. ii./103,1493.* See also Williams'.

* **Peslam.**—Analysis showed approximately Zinc Oxide 12, Flowers of Sulphur 8, Maize Starch 18, Salicylic Acid 1.5, Oil of Cade (?) 1.5, Oil of Birch Tar 8, Anhydrous Lanoline 25.5, Soft Paraffin 25.5%.—*B.M.J. ii./10,1353.*

* **Powell's Balsam of Aniseed.**—Used to contain Morphine but does not now.—*C.D. i./13,650.*

The Manufacturers inform us it contains no ingredient coming within **PI**, or **P** Parra detected an active ingredient not given in S.R.—*C.D. i./13,503.*

* **Pritchard's Teething and Fever Powders.**—Dose on lines of Stedman's v. infra. Average weight 2.1 grains. Consist of Calomel 47, Antimony Oxide 0.7, Calcium Phosphate 1.4, Milk Sugar 50.9%.—*B.M.J. ii./108,1022.*

* **Quina Wine.**—Alcohol 16.9%, Glucose 22.2%, Alkaloid Cinchona (0.05). "Two measures" represent about 10 to 15 minims Liquid Extract of Cinchona.—*B.M.J. i./109,1308.*

* **Radol Cancer Cure.**—"An Acid Solution of Quinine"—*P.M.C.R.*

* **Reudel Bath Saltrates.**—Magnesium Carbonate 0.005, Calcium Carbonate 0.005, Potassium Carbonate 0.00125, Calcium Sulphate 0.0025, Sodium Chloride 0.0012, Lithium Carbonate 0.00005, Borax 0.10, Sodium Bicarbonate 0.305, Sodium Carbonate 0.50, Hydrogen Sulphide 0.025, "Baregine" 0.025, "Oxygenated Salts" 0.03, Radio-active substances traces, Aromatic Essence sufficient quantity.—*L. i./24,256.* (As sold in Italy.)

* **Roche's Embrocation.**—Olive Oil, Oil of Amber, Oil of Cloves, and Oil of Lemons.—*Murrell.*

According to *L. i./24,256.*—Oil of Cloves, Oil of Amber, Oil of Lemon, of each 15, Olive Oil 55. (As sold in Italy.)

* **Ruspini's Styptic.**—A strong solution of Gallic Acid and Spirit of Roses, with perhaps a little Zinc Sulphate.—*Murrell.*

* **St. Jacob's Oil.**—Turpentine 60, Ether 25, Camphor 10, Alkanet Root 25.—*L. i./24,256.* (As sold in Italy.)

* **St. Raphael Tonic Wine.**—"Quinquina."—Alcohol 16.89, Glucose 11.8, Alkaloid (Cinchona) 0.008. A wine-glassful = about $1\frac{1}{2}$ m of Liquid Extract of Cinchona.—*B.M.J. i./109,1308.*

* **St. Raphael Tannin Wine.**—Alcohol 14.65, Glucose 14.0, Tannin (as in ordinary Port Wine), Alkaloid a trace.—*B.M.J. i./109,1309.*

* **Salrado Concentrated (Tokalon).**—"The active constituents of Cascara, Ginger and Gentian" with Caffein 0.30, Lithia 0.5 per cent.—*L. i./24,256* (As sold in Italy.)

* **Sargol.**—"A Flesh Producer." Analysis of the Tablets (average weight 5.3 grains) showed Zinc Phosphide 0.7, Lecithin 1.9, Calcium Hypophosphite 12.9, Sodium and Potassium Hypophosphites 7.7, Albumen (Soluble) 4.2, Insoluble Protein (? Coagulated Albumen) 10.8, Sugar 18%.—*B.M.J. i./12,846.*

The following formula is given:—Ext. Saw Palmetto 2 grains, Calcium Hypophosphite $\frac{1}{2}$ grain, Sodium Hypophosphite $\frac{1}{4}$ grain, Potassium Hypophosphite $\frac{1}{4}$ grain, Lecithin $\frac{1}{2}$ grain, Ext. Nux Vomica $1/12$ th grain.—*L. i./20,1275.*

* **Sarvar's Coca Wine.**—Alcohol 23.4%, Glycerin 6.1%, Glucose 2.6, Alkaloid (Coca) 0.07%. Dessertspoonful = about 21 minims of Liquid Extract of Coca.—*B.M.J. i./109,1307.* Makers say this is **PI**

* **Scott's Pills.**—Average weight 2.4 grains. Examination indicated small quantity of Aloes, Ginger, Rhubarb and Soap.—*B.M.J. i./11,1326.*

* **Scott's Emulsion** is stated to have the following composition: Cod-liver Oil 40 litres, Glycerin 19.875 kilos, Solution of Calcium Hypophosphite 0.8 per cent., 20.450 kilos, Solution of Sodium Hypophosphite 0.4 per cent., 20.150 kilos, Flavouring Essences 2.970 kilos, Gum 650 Gm.—*Ph. Notes.*

According to *L. i./24,256.*—Cod Liver Oil 44, Glycerin 16. Sol. Calcium Hypophosphite (1.25 per cent.) 20, Sol. Sodium Hypophosphite (0.625 per cent.) 20, Alcohol, Tragacanth, Essential Oils, sufficient quantity. (As sold in Italy.)

Seeger's Hair Dye.—W. (Brown) Pyrogalllic Acid 3·8%, Cupric Chloride (anhydrous) 1·8%, Hydrochloric Acid (B.P.) 0·7%, Sulphuric Acid 0·07%.—*B.M.J. i./10,152.*

*** Seigel's (Mother) Syrup.**—

A Government chemist, acting upon instructions from the House of Commons Committee on Patent Medicines, 1914, found:—

“**ORGANIC INGREDIENTS.** The proportion of sugars represents about 40 per cent. of Treacle. In addition to the sugars the organic ingredients were found to include:—

Essential Oil having an odour of Sassafras, a small quantity; Starch, a small quantity; Acetic Acid, 0·66 per cent.; Capsicum, equivalent to about 1 per cent. of Tincture of Capsicum B.P.; Aloes, about 1 per cent. Other vegetable extractive substances (after deducting 1·4 per cent. of extractives due to Treacle) 7·8 per cent.

MINERAL INGREDIENTS consisted of borax with small quantities of chlorides, sulphates and phosphates such as occur in the ashes of vegetable substances:—

Total Boric Acid 2·12 per cent. (equivalent to 3·36 per cent. of crystallised borax). Total chlorides 1·51 per cent. (calculated as hydrogen chloride).

ACIDS. The volatile acid consisted mainly of acetic acid with a little boric acid. The total free acid of the sample in terms of hydrochloric acid is 1·12 per cent., equivalent to 10·6 per cent. of the B.P. Dilute Hydrochloric Acid.

The proportion of free acid, other than acetic acid, would correspond with 0·72 per cent. of hydrochloric acid, equivalent to 6·8 per cent. of the ‘diluted hydrochloric acid’ of the Pharmacopœia. Very little of this hydrochloric acid, however would be actually present in the ‘free condition.’—*Lancet Supp. on Sale of Patent Medicines, Jan 10, 1925, 11.*

Previous information, *Edition XVII, Vol. II., p. 577.*

Serravallo's Tonic Bark and Iron Wine.—Alcohol 17·26%, Glucose 6·8, Cane Sugar 12·2, Iron 0·01, Alkaloid (Cinchona) 0·05, Liqueur glass represents about 3 minims of Liquid Extract of Cinchona.—*B.M.J. i./09,1308.*

*** Sequarine.**—The liquid contained Alcohol 35·8%, Oil of Peppermint a trace; on evaporation it left 1·9 per cent. solid residue of which 0·6 was ash,—principally Sodium and Potassium Phosphates. Nitrogen present 0·22 per cent. = to 1·4% of Protein, small portion present as Ammonia, perhaps formed by decomposition of nitrogenous organic matter. Definite constituents could not, of course, be isolated.—*B.M.J. i./11,27.*

Shadeine (Brown).—Pyrogalllic acid 2·1%, Cupric Chloride (anhydrous) 1·3%, Hydrochloric acid (B.P.) 0·3%.—*B.M.J. i./10,152.*

Singleton's Eye Ointment.—Analysis showed principal ingredient was Red Mercuric Oxide 7·4. Fatty basis contained inter alia about 4% beeswax.—*Secret Remedies.*

*** Smedley's Chilli Paste.**—Powdered Capsicum 4, Lard 60, Alkanet Root 1.—*L. i./24,256. (As sold in Italy.)*

*** Stearn's Headache Cure.**—Powders each contained Acetanilide 3·92 grains, Caffeine 0·98 grain, Milk Sugar 4·9 grains.—*B.M.J. ii./06,27.*

*** Stedman's Teething Powders.**—Average weight 2·4 grains. For a child under 3 months the third of a powder; from 3 to 6 months $\frac{1}{2}$ a powder; when above 6 months a whole powder. The powder consists of Calomel 29% and Sugar of Milk 71%. A trace of alkaloids (not identified).—*B.M.J. ii./08,1022.*

*** Steedman's Soothing Powders.**—Calomel and Starch.—*L. ii./03,1493.* Average weight 2·8 grains each. Consisted of Calomel 27, Sugar 22, Maize Starch 50·5, Ash 0·5%. Directions similar to Stedman's above.—*B.M.J. ii./08,1022.*

Australian Customs require statement on the labels “The contents of this package include 27% Calomel.” ‘Calomel has induced sleep.’ Opium is not present in any form.—*P.M.C.E., C.D. i./13,232; B.M.J. i./13,350.*

*** Tatcho.**—Borax 2·7%, Glycerin 2·5%, Quinine 0·006%, Formaldehyde Solution (40%) 0·38%, colouring and perfume a trace, Alcohol 2·4%, Water to 100, by volume.—*B.M.J. i./10,151.*

*** Therapion No. 3.**—Results indicated Camphor 2·5, Glycerin 24, Powdered Liquorice 40, Calcium Glycero-phosphate 1·8, Extract of Gentian 5, Extract of Damiana (?) 8, Alkaloid 0·06, Water to 100.—*B.M.J. i./09,32.*

The Manufacturers inform us ‘non-poisonous.’

*** Towle's Pennyroyal and Steel Pills.**—Contain about 14 grains Dried Iron Sulphate, Capsicum 86 grains, Pennyroyal Oil 3 minims, excipient $\frac{1}{2}$ ss.—in 100 pills.—*B.M.J. ii./07,1653.*

Trommer's Elixir.—Stated to contain the active enzymes of Malt,

Glycerophosphates, and what is described as the "alkaloidal" extractive of Cod livers.—*L. i.*/10,653.

Trommer's Malt Extract and Cod Liver Oil.—Oil 29.9%. Reducing Sugars (as Maltose) 41.4%. Protein 2.4%. Diastatic Power 35.—*B.M.J. i.*/10,30

ⓈⓈ ***Tucker's Asthma Cure.**—According to Dr. Willcox, Home Office Analyst, in the action against the "*Lancet*," January, 1908, this contains Cocaine 2.28 grains, Atropine 0.87 grain, Sodium Nitrite 15.25 grs. per ounce, 20-30% Glycerin and a trace of Balsam or Benzoin.

A solution of Cocaine Nitrite 1.028, Atropine Nitrite 0.581 in Glycerin 32.16 and Water to 100 is said to produce good results when used in an atomizer. The Nitrites in question are not very stable salts.

Another analysis says Atropine Sulphate 0.15, Sodium Nitrite 0.6, Glycerin 2.0 Water 15.00.—*B.M.J. i.*/09,43.

Vasey, for the "*Lancet*," found in one sample Cocaine 1.03 grains. Atropine 0.52 grains Sodium Nitrite 16 grains: in another, Cocaine 1.47 grains, Atropine 0.66 grains, Sodium Nitrite 24.46 grains.—*C.D. i.*/08,112; *B.C.D. i.*/08e 73, cf. also *L. ii.*/03,1493.

The alkaloids in such a mixture may be determined by means of Platinic Chloride and estimating the Nitrogen in the precipitate,—then differentiating Cocaine from Atropine by precipitation with Potassium Dichromate Solution in strong Hydrochloric Acid.

Another method would be to soak up the fluid in a paste of Lead Oxide and Magnesium Oxide, extract repeatedly with Chloroform, filter, evaporate to dryness, weigh total Alkaloids, then titrate with N/100 Acid (using Phenolphthalein); this gives the amount of Atropine; finally titrate with Methyl Orange, which gives Cocaine.

Van Vleck's (Dr.) Absorptive Plasma.—Formula approximately: Powdered galls, 6 parts, Menthol 1 part, Crude Petroleum Jelly to 100 parts.

***Vana.**—Alcohol 19.2, Glucose 20.0, Alkaloid (cinchona) 0.23, Calcium 0.01 Phosphorus (combined) as Phosphoric Acid 0.13. A wineglassful = about 3 minims of Cinchona Extract (Liq.).—*B.M.J. i.*/09,1308.

***Varalettes (Bishop's Gout)** showed presence of Lithium Citrate and a small quantity of what appeared to be Piperazine with the usual effervescent basis — "Secret Remedies."

***Veno's Lightning Cough Cure.**—*Veno's Lightning Cough Cure* contains about 8% Glycerin, with small quantities of Alcohol, Chloroform and Resin.—The Government Chemist's evidence before the P. Med. Committee 1914.—*L. Supp.*, 10/25,11. See also previous analysis, 17th. Edn., Vol. II., p. 579.

***Vibrona—a Wine of Cinchona.**—2 fluid ounces represent 5 grains of Cinchona Bark, the total alkaloids being in the form of Hydrobromides. A tonic preparation well adapted for use in cases of debility and nervous prostration.—*B.M.J. The late B. H. Paul* had the wine under systematic analytical supervision.

***Virol.**—Analysis showed it to contain Fat 12.3%, Reducing Sugars (as Maltose, 59%), Diastatic power nil.—*B.M.J. i.*/10,29.

Vitæ-Ore.—According to analysis each dose would contain Ferric Oxysulphate 0.47 grain and Magnesium Sulphate Anhydrous 0.15 grain.—*B.M.J. i.*/11,27.

Wallace's Twelve Specific Remedies.—No. II. Analysis showed Berberine 0.05, Hydrastine 0.11, Alcohol 32.3 by volume, Extractive 2.7, Ash 0.8. No. III. Analysis showed Caffeine 0.25, Cane Sugar 1.7, Glucose 0.6, Ash 0.52. Alcohol 47.25 by volume, Extractive 3.13%. A Tincture of pale roasted coffee (1 to 5) appeared to be identical. No. V., Alcohol 30.5 by volume, Ash 0.2, Reducing Sugars 2.9, Extractive 1.7. No. VII., Alcohol 51.05, Ash 0.22, Reducing Sugar 1.0, Fat and Extractive 2.1. A Tincture of Nutmeg (1 to 5) was found to agree in all respects. No. X., Alcohol 26.6, Ash 0.38, Reducing Sugars 0.55, Extractive 1.27. Very like weak Arnica Tincture. No. XI., Caffeine 0.1, Sugars (chiefly cane sugar) 0.7, Ash 0.26, Alcohol 51.05, Extractive 2.1. On same lines as No. III.—*B.M.J. i.*/11,147.

***Warner's Safe Cure.**—Potassium Nitrate (about 10 grains to the ounce) and various diuretic herbs.—*L. ii.*/03,1493. A mixture made with Potassium Nitrate 50 grains, Alcohol 5 drachms, Gaultheria Oi $\frac{1}{2}$ minim, Liquid Extract of Taraxacum 10 drachms, Glycerin 4 drachms, and Water to 8 ounces is almost identical.—*B.M.J. i.*/07,213. An Extract of Liverwort Leaves 30, Nitre 15, Glycerin 45, Alcohol 60, with some Wintergreen Oil. Pills.—Aloes, Soap, Marsh Mallow, and Liquorice.—*B.M.J. ii.*/08,1377.

See also formula presented to German Government authorities by manufacturer.—*M.P.*, Sept. 29/09,347.

* **Welch's Female Pills.** (*Kearsley's original Widow Welch's Female Pills*).—Contain Iron Sulphate, Sulphur, Liquorice, Turmeric with excipient.—*B.M.J.* ii./07,1654.

* **Whelpton's Purifying Pills.**—Weight $2\frac{1}{2}$ grains. Chemical examination showed Aloes (apparently Socotrine). Powdered Colocynth, Ginger and Gentian. No evidence of Mercury or Calomel.—*B.M.J.* i./11,1326.

* **Williams' (Dr.) Pink Pills for Pale People.**—Contain Potassium Carbonate, Iron Sulphate and traces of Manganese Oxide and 'Neuræmin' (supposed to be a combination (?) of lecithin, hæmatin, and smilacin); the last is from Sarsaparilla; also a substance containing Emodin. Some Arsenic is contained in some.—*B.M.J.* i./07,879.

The quantities found indicated the following formula—exsiccated Sulphate of Iron 0.75 grain, Potassium Carbonate 0.66, Magnesia 0.09, Powdered Liquorice 1.4, Sugar 0.2, in one pill.—*B.M.J.* i./09,32. See also *B.M.J.* i./10,213.—Formula may have been altered.

* **Wincarnis**, see Colman's.

* **Winslow's, Mrs., Soothing Syrup.**—Previously contained poison, but in November, 1909, was altered—does not come within provisions of Poisons and Pharmacy Act, 1908. cf. *C.D.* i./13,650.

Analysis showed it to contain in 100 parts by measure, Potassium Bromide 2.0, Alcohol 4.3 parts by measure, Essential Oil (Anise) about 0.1 part. Sugar 56.5 parts, Emodin was present in small quantity, a Syrup containing 1.2% by measure of the Syrup of Senna (Off.), agreed in several respects.—*B.M.J.* i./12,683.

Woodcock's Pills.

* **Woodcock's Wind Pills.**—Aloes, Caraway Oil and Soap.—*L.* ii./03,1493; *B.M.J.* i./11,1326 gives the following:—Freed from coating the pills had an average weight of 1.6 grains. Evidence of the presence of Aloes (Barbados) or a preparation of aloes, a little Ginger, a little Soap, a trace of Capsicum and Oils of Peppermint and Cinnamon, and some indistinguishable vegetable tissue.

Wooldridge's Gout and Rheumatic Tincture caused death owing to having been taken in overdose; the ingredients contain Colchicum. The intestines were much inflamed.—*W. W. Westcott's Coroner's Case.*—*P.J.* i./13,17.

Woodward's *Gripe Water.—Analysis showed in 100 parts by measure Sodium Bicarbonate 1.08, Essential Oil about 0.03, Alcohol 3.8 parts by measure, Sugar 20.5. The Essential Oil appeared to be chiefly Oil of Caraway, with a little Oil of Dill, and possibly also of Anise.—*B.M.J.* i./12,683.

"The most important constituent is omitted in the S.R. analysis and those given are inaccurate."—*Umney, P.M.C.E., P.J.* ii./12,582; *C.D.* ii./12,721.

Government analyst, it was stated, failed to find an ingredient and he found certain ingredients that are not contained,—his report on analysis being:—

Alcohol 3.35, Sugar 18.87, Mineral constituents, chiefly sodium bicarbonate, 0.92, Essential Oils 0.04, Capsicum Extract a trace, Water 76.82.

The figures are percentages by weight. The mineral constituents in addition to sodium bicarbonate included magnesium, calcium, and potassium, amounting to 0.08. These are probably adventitious, and due partly to the sugar and partly to the water. The quantity of essential oils is too small for chemical determination, but the constituents, judging chiefly by odour, consisted mainly of the oils of caraway and dill.

Umney's Evidence, P.M.C.E., C.D. ii./12,890; *P.J.* ii./12,750. Government Analyst communicated with replied 'No reason whatever to modify terms of report.'—*C.D.* i./13,231, see also *E. J. Parry, ibid.*, p. 563.

Harrison admits trace of pungent aromatic substance.—*B.M.J.* i./13,947; *C.D.* i./13,651.

The Trade Mark under which this preparation is sold was the subject of legal proceedings. The rights in the mark by William Woodward, Ltd., were upheld.—*P.J.* i./15,315,337.

* **Zam-Buk.**—Eucalyptus Oil 14%, Pale Resin (Colophony) 20%, Soft Paraffin 55%, Hard Paraffin 11%, Green colouring matter, a trace.—*B.M.J.* i./08,944

* **Zotos.**—Capsules (sea sickness preventive), contained 6.3 grains, pinkish powder consisting of 76.9% Chlorbutol (Syn. Chloretone), and 23% Lactose.—*B.M.J.* ii./09,1419.

* **Zex Powders.**—Average weight $4\frac{1}{2}$ grains. Consists of Aectanilide only.—*B.M.* i./08,1112

For Remedies not in the list see note at commencement of chapter.

STAINS, TO REMOVE.

Stains.	On cloth. Removed with :—	On the skin. Removed with :—
Acid Pieric	Sodium Carbonate Solution, hot.	Sodium Benzoate Solution.
Acid Pyrogallie	First moisten with Ferrous Sulphate, and then wash in Oxalic Acid Solution	On fingers, use Pot. Carb. 1 oz., Calx Chlor. $\frac{1}{2}$ oz. water 4 ozs. Or add 1 or 2 dr. of Sulphuric Acid to $\frac{1}{2}$ pint 25% Sod. Sulphite Sol.; $\frac{1}{2}$ oz. of this c. 4 ozs. water.—P.J. i./20,616.
Acridavine	Dilute HCl. and bleach after.	Ammonium Persulphate Solution is also good.
Bremine	Liquor Sodæ (Caustic Soda Solution).	Sulphurous Acid, or dil. H ₂ SO ₄ and spirit.
Carbol Fuchsin	Sulphuric Acid and water. Repeat several times if necessary.	Dilute Ammonia Solution, or Carron Oil.
Cascara (Liq. Ext.)	Ammonia	Sulphuric Acid and water.
Cochineal	Hot water	Soap and water.
Crocus (Saffron)	Wash with HCl. and boil with Washing Soda.	Washing Soda in water
Eosin	Strong Hydrochloric Acid	Strong HCl.
Ferric Chloride	Oxalic Acid Solution ..	As for cloth.
Gentian Violet	H ₂ SO ₄ Dil. and Hypochlorite as bleach after.	Spirit.
Hæmatoxylon (Logwood) ..	Render acid and then alkali, and bleach.	Make alkaline and wash with Hypochlorite.
Henna	HCl. and hot water. ..	Use Hypochlorite.
Ink, black	Oxalic Acid, and finally bleach with Hypochlorite	Soap and water.
(The two-solution ink (2) Oxalic Acid Solution.)		of (1) Chlorinated Lime
Ink, red (if made with Eosin).	Hydrochloric Acid, and wash well.	Soap and water.
(All best red ink is made with Eosin).		
Ink, typewriting (purple).	Dilute Hydrochloric Acid	As for cloth.
Iodine, Tincture of	15 to 20% warm Hypo. solution.	
Methylene Blue	Wash c. H ₂ SO ₄ Dil. and use Hypochlorite after. Spirit also helps.	Spirit removes easily.
Potassium Chromate	Washes out with water	Soap and water.
Pot. Permang.	Sulphurous Acid	Ac. Tart., HCl. SO ₂ or Hypo.
Rhubarb	Hot soap wtr. Bleach.	Soap and water.
Rosein Acetate	Wash c. H ₂ SO ₄ Dil. and bleach after.	Spirit, strong.
Silver Nitrate	Wash c. solution of Iodine 2, Pot. Iod. 10, Liq. Ammonia 1, Water 100, allow to soak in, then rinse c. Ammonia.—P.J. ii/28,206.	As for cloth.
Tobacco stains		Chlorinat Soda sol. or Pot. Permang.—followed by SO ₂ .—P.J. ii/28,312,342.
Walnut Juice	Hot water and soap ..	Soap and water.

ANALYSIS OF PRESCRIPTIONS.

The late W. Martindale published an analysis of 12,000 prescriptions in 1894. The following, giving the frequency per 1000 of some of the most popular medicamenta compared with figures published in 1913, is of interest.

	12,000 pre- scriptions from Aberdeen, Bournemouth, Carlisle, Cork, Oxford & Lon- don. W. Mar- tindale, 1894.	2,000 London prescriptions. W. Martin- dale, 1894.	1,000 London prescriptions compiled by B. Cockburn, <i>P.J. i./13,290.</i>
Spiritus Chloroformi ..	93.1	91.0	113
Sodii Bicarbonas ..	67.3	69.5	97
Tinct. Nucis Vom. ..	82.6	73.0	91
Aq. Chloroformi ..	36.5	86.5	90
Spirit Ammon. Aromat. ..	56.3	58.0	75
Glycerin ..	72.9	65.0	68
Aqua Menth. Pip. ..	31.0	17.5	60
Liq. Strych. Hydrochlor. ..	31.0	34.0	56
Syrup Aurant. ..	66.3	64.5	48
Sod. Salicyl. ..	27.0	19.0	37
Liq. Arsenicalis ..	29.3	24.0	36
Potass. Bicarb. ..	38.6	28.0	36
Potass. Bromid. ..	30.4	29.0	34
Ammon. Carb. ..	33.1	37.5	33
Potass. Iodid. ..	29.7	24.5	31
Tinct. Card. Co. ..	25.4	30.5	31
Quin. Sulph. ..	49.8	39.5	28
Tinct. Aurant. ..	16.2	25.5	26
Mag. Sulph. ..	21.9	22.5	26
Syr. Tolu ..	26.0	19.0	25
Acid Boric ..	32.5	39.0	24
Tinct. Camph. Co. ..	26.3	18.5	24
Inf. Gent. Co. ..	19.6	21.5	23
Pot. Cit. ..	12.6	25.0	22
Ext. Bellad. ..	25.1 (virid)	34.0 (virid)	21
Ext. Nucis Vom. ..	24.7	30.0	21
Aq. Rosæ ..	13.8	18.0	18
Acid Carbolie ..	12.0	10.5	17
Acid Hydrochlor. ..	11.5 (dil.)	9.5 (dil.)	17
Mucilago ..	16.0	12.5	17

—W. H. M., *P.J. i./13,354.*

For an Analysis of 185,000 *Insurance Prescriptions in Scotland for 'Dangerous Drugs'* see Vol. I., p. 1015.

It was decided to repeat an investigation of the kind for a **winter month** in Scotland.

During March, 1923, of 234,868 prescriptions and 991 Emergency Orders under the N.H.I. throughout Scotland, 14 lbs. of *Opium* and preparations containing *Opium* expressed in terms of *Opium Powder*, 2½ lbs. *Morphine* and its preparations expressed in terms of *Alkaloid*, 1,416 grains of *Cocaine* and preparations expressed as *Alkaloid* and 2,925 grains of *Diamorphine* and preparations (in terms of *Diamorphine Hydrochloride*) were prescribed.—A. B. Gilmour, Superintendent Central Checking Bureau, Glasgow, Sept., 1923.

GLOSSARIES.

ARABIC GLOSSARY.

NOTE.—This was specially compiled for us by W. R. Robb while serving with H.M. Forces during the war, from the language actually spoken in the Tigris valley, and differs slightly from that spoken in Syria and Egypt. It might therefore be termed pure Mesopotamian.

H. C. Sinderson, Physician to the New General Hospital, Baghdad, was good enough to amend certain items and add to the Glossary—1922. We acknowledge the suggestions gratefully.

<i>Aboo Sufar</i> , jaundice.	<i>Henitch</i> , chin.
<i>Aboo Zowwa</i> , cholera.	<i>Ichasm</i> , nose.
<i>Adalah</i> , muscle.	<i>Id</i> , hand.
<i>Adwa</i> , contagion.	<i>Ighma</i> , faint.
<i>Adhwawi</i> , jackal bite.	<i>Iridje</i> , vein.
<i>Akab</i> , heel.	<i>Irr</i> , penis.
<i>Akrash</i> , dumb.	<i>Ishal</i> , diarrhoea.
<i>Ameë</i> , blind.	<i>Itches</i> , elbow.
<i>Araj</i> , lame.	<i>Ithin</i> , ear.
<i>Asab</i> , nerve.	<i>Jidam</i> , foot.
<i>Athm</i> , bones.	<i>Jidiri</i> , small pox.
<i>Atrash</i> , deaf.	<i>Jifn</i> , eyelid.
<i>Bahim</i> , thumb.	<i>Jild</i> , skin.
<i>Baydh</i> , testicles.	<i>Jimah</i> , fist.
<i>Bug</i> , mosquito.	<i>Jised</i> , body.
<i>Buttin</i> , abdomen.	<i>Jurra</i> , wound.
<i>Cashuggar</i> , spoon.	<i>Kabath</i> , constipation.
<i>Chab</i> , ankle.	<i>Kanakina</i> , quinine.
<i>Chef</i> , palm.	<i>Kebed</i> , liver.
<i>Chud</i> , cheek.	<i>Kessr</i> , fracture.
<i>Dam</i> , blood.	<i>Khastakhana</i> , hospital.
<i>Demboos</i> , pin.	<i>Khedma</i> , bruise.
<i>Dihn</i> , oil.	<i>Kilwa</i> , kidney.
<i>Dihn Zait</i> , olive oil.	<i>Kitif</i> , shoulder.
<i>Dihn Kharwa</i> , castor oil.	<i>Lesha</i> , dead body.
<i>Dimagh</i> , brain.	<i>Lissan</i> , tongue.
<i>Dowa</i> , medicine.	<i>Ma-ada</i> , stomach.
<i>Dra</i> , arm.	<i>Machloob</i> , hydrophobia.
<i>Dukk</i> , phthisis.	<i>Mai</i> , water.
<i>Dumbila</i> , sore.	<i>Madjrook</i> , wounded.
<i>Ejzachi</i> , chemist.	<i>Magnoon</i> , insane.
- <i>Ek</i> or - <i>tek</i> as a suffix signifies "your." Thus "Hazurtek" means "your side."	<i>Maljeedoo</i> , arm sling.
<i>Eyein</i> , eye.	<i>Mardh</i> , illness.
<i>Fachud</i> , hip.	<i>Marham</i> , ointment.
<i>Firash</i> , bed.	<i>Masareen</i> , bowels.
<i>Frengi</i> , syphilis.	<i>Masmoom</i> , poisonous.
<i>Gacha</i> , cough.	<i>Middah</i> , pus.
<i>Galub</i> , heart.	<i>Mitchloob</i> , hydrophobia.
<i>Gharghara</i> , gargle.	<i>Nafas</i> , breath.
<i>Goosa</i> , forehead.	<i>Nezhla</i> , catarrh.
<i>Hab</i> , pill or tablet.	<i>Racheta</i> , prescription.
<i>Hajib</i> , eyebrow.	<i>Rass</i> , head.
<i>Hakeem</i> , doctor.	<i>Ridjla</i> , leg.
<i>Halk</i> , mouth.	<i>Rimsh</i> , eyelash.
<i>Harq</i> , burn.	<i>Rookoboy</i> , knee.
<i>Hasbah</i> , measles.	<i>Rugba</i> , neck.
<i>Hasura</i> , side.	<i>Rusook</i> , wrist.
<i>Hazurtek</i> , your side	<i>Safra</i> , bilious.
	<i>Saheyah</i> , sanitary department.
	<i>Sayarat-es-sahha</i> , ambulance.

Arabic Glossary—continued.

Schoona, fever.
Schladt, bandage.
Shar, hair.
Sheesha, bottle.
Shiffaf, lips.
Shrunka, syringe.
Simm, poison.
Sin, tooth.
Soof, wool.
Spirtoo, methyated spirit.
Sudra, chest.
Susanak, gonorrhœa.
Taharl, spleen.
Tenteryoke, tincture of iodine.
Thahr, back.

Toze, powder.
Ukhut, Baghdad boil (oriental sore).
Uja, pain.
Urther, finger nail.
Usbah, finger.
Usbah ridjla, toe.
Waja rass, headache.
Warram, swelling.
Widja, face.
Yimina, right hand.
Yissira, left hand.
Yukos, cut.
Zerdoom, throat.
Zibb, penis.
Zowwa, vomit.

BELGIAN GLOSSARY.

Belgian prescriptions are written in Latin or French (vide French Glossary) or a mixture of both languages. For a note on Belgian prescriptions by V. Renneboog, see C.D. i./15,362.

DANISH GLOSSARY.

Aandedrag, breathing.
Aare, vein.
Aare-Indsprøjtning, intravenous injection.
Atomsprøjte, spray or atomiser.
Badevand, lotion (lit. bath water).
Badning, fomentation.
Blære, blister.
Blandes, to be mixed.
Belægges (Piller), to be coated (pills).
Børstes, to be brushed.
Brækmiddel, emetic.
Citronsaft, lemon juice
Daglig, daily.
Den smærtefulde Del, the painful part.
Dessertskefuld, dessertspoonful.
Draaber, drops.
Døgn, the space of 24 hours.
Efter Maaltid, after meals.
Etiket med Anvisning, label with formula.
Flaske, bottle.
Forkø'else, cold
Forsø'les (Piller) to be coated (pills)
Fortyndes, to be diluted.
For udvortes Brug, for external use.
Før Maaltid, before meals.
Gift, poison.
Glas Kapsler eller smaa Flasker, glass capsules or ampoules.
Glasstang, glass rod.
Gnidning, friction.
Gummerne, the gums.
Gurglevand, gargle.
Haarvand, hair-lotion.
Hjærte, heart.
Høstemixtur, cough-mixture.
Hovedpine, head-ache.

Hud-Indsprøjtning, subcutaneous.
Hver anden, every two.
Hver tredje, every three.
Igle, leech.
Ikke, not.
I lige Dele, of each equal parts.
Indaanding-indaader, inhalation inhaler.
Indgnid, rub.
Indgnides, to be rubbed.
Indgydes, to be instilled.
Indsprøjtjes, to be injected.
Indsprøjtning, injection.
I Vægt, by weight.
Klystér, enema.
Knuses eller brækkes to be crushed or broken.
Kop, cup.
Krukke, pot.
Latverge, electuary.
Lige Dele, equal parts.
Ligtorn, corn.
Mælk, milk.
Mellem, between.
Moderkrans, pessary.
Mundvand, mouth-wash.
Muskel-Indsprøjtning, intramuscular injection.
Nat, night.
Næse, nose.
Næsebor, nostrils.
Omrystes, shake (the bottle).
Omslag, poultice.
Ophlæsning, flatulence.
Opløse, dissolve.
Opsnuses gennem Næseborene, to be sniffed up the nostrils.
Pensle, paint (lit. pencil).
Pensles, to be painted.
Rystes, shake (the bottle).

Danish Glossary—continued.

Signatur, label (medical label).
Skefuld, spoonful.
Smærte, pain.
Som foreskrevet, as directed.
Spiseskefuld, tablespoonful.
Sprøjte, syringe.
Stikpille, suppository.
Straks, at once.
Tages, to be taken.
Tandmiddel, dentifrice.
Teskefuld, teaspoonful.
To Gange, twice.

Tre Gange, three times.
Ved Sengetid, just before retiring to rest (lit. at bed-time)
Vekselsvis, alternately.
Vægt, weight.
Øjendraaber, eye-drops.
Øjelaag, eye-lids.
Øjenhaar, eye-lashes.
Øjenskaerm, eye-shade
Øjenvand, eye-wash
Ørepine, ear-ache

DUTCH GLOSSARY.

Ademhaling, breathing.
Ader, vein.
Bedecken (pillen), to be coated (pills).
Besproeiingstoestel, atomiser or spray
Bestrijken, to be painted.
Blaar, blister.
Baarmoederkrans, pessary
Braking, vomiting.
Citroensap, lemon juice
Dagelijks, daily.
De flesch, bottle.
Dicht bij, near to.
Den volgende morgen, the next, or following morning.
Droppels or *druppels*, drops.
Etiket met recept, label with formula.
Gebruik, use, application.
Gedurende het bruisen, during effervescence.
Gegruisd of in stukjes gebroken, to be crushed or broken.
Gelijke deelen, equal parts.
Glazen capsules, glass capsules or ampoules.
Glazen staafje, glass rod.
Goedgeschudden, to be well shaken (the bottle).
Gorgelen, gargle.
Het pijnlijk deel, the painful part
Het tandvlesch, the gums.
Hoest, de, the cough.
Inademing-respirateur, Inhalation-inhaler.
Indien het hoesten lastig is, when the cough is troublesome.
Indruppelen, to be instilled.
Inspuiting binnen de spieren, intramuscular injection.
Inspuiting binnen de aderen, intravenous injection.
Inspuiting onder de huid, subcutaneous injection.
Klister spuit, enema
Kokend, boiling.
Kopje, cup.
Melk, milk.
Met mate, moderately.
Mondspoeling, mouth-wash.

Na den maaltijd, after meals.
Neertiggende (rustende), lying down.
Niet te gebruiken, not to be taken.
Om de beurt, alternately.
Om op te snuiven, to be sniffed up the nostrils.
Onmiddellijk, immediately.
Ooghaartjes, eye-lashes.
Oogkapje, eye-shade.
Oogleden, eye-lids.
Oogwassching, eye-wash.
Ook, also.
Op de gebruikelijke wijze, in the usual manner (as taken before).
Papmiddel, fomentation.
Per gewicht, by weight.
Plaatselijk aan te wenden, for local use only.
Potje, pot.
Prikkelend, irritable.
Purgeerend stropje, electuary.
Spoeling voor de oogen, eye-wash.
Steekpilletje, suppository.
Sproeier, spray.
Spuit, syringe.
Stopfel van pluksel, tampon.
Tabletje, tablet.
Tandpoeder, dentifrice.
Van elk evenveel, of each equal parts
Verdeeld in gelijke deelen, let it be divided into equal parts.
Vergift, poison.
Verzilveren (pillen), to be silvered (pills).
Volgens het voorschrift, as directed.
Voor het naar bed gaan, just before retiring to rest.
Voor inspuiting, to be injected.
Voor inwendig gebruik, for internal use.
Voor uitwendig gebruik, for external use.
Waskaars, bougie.
Winderigheid, flatulence
Wrijven, rub.
Wrijving, friction.
Zonder, without.
Zoo noodig, if necessary.

FRENCH GLOSSARY.

argenter (pilules), to be silvered (pills).
baisse-langue, tongue-depressor.
broyer ou concasser, to be crushed or broken.
dragéifier (pilules), to be coated (pills).
être instillé, to be instilled.
moins que, unless.
impoucle, blister.
après les repas, after meals.
au-dessus, above.
au poids, by weight.
avant les repas, before meals.
Baguette en verre, glass rod.
Bande, a bandage.
Bandage, a truss.
Biberette, feeding cup.
Bien, well.
Bien agiter le flacon, the bottle to be well shaken.
Boire, drink.
Bougie, a catheter.
Bouillant, boiling.
C.à.c., à.d., à.s. = *cuillerée à café*,
à dessert, à soupe, q.v.
Chaque jour, daily.
Charpie, lint.
Chauffé, warmed.
Cils, eye-lashes.
Cœur (le), the heart.
Collyre, eye-wash.
Comme il a été prescrit, as directed
Compte-gouttes, a small glass tube to count drops.
Coqueluche, whooping cough.
Coricide, corn solvent.
Coton hydrophile, absorbent wool.
Crépine et pulvérisateur, spray and atomiser.
Cuillerée, spoonful.
Cuillerée à café, teaspoonful.
Cuillerée à dessert, dessert-spoonful (10 gm.).
Cuillerée à soupe, tablespoonful.
Cuillerée à thé, teaspoonful (*ou à café* —5 gm.).
Cuillerée ordinaire, tablespoonful (15 gm.).
Cuir, leather.
De bonne heure demain, early to-morrow.
De jour en jour, from day to day.
De la façon habituelle, in the usual manner.
De la façon prescrite, in the manner directed.
Demain matin, to-morrow morning.
Demain soir, to-morrow night.
Demis, dislocated.
De temps en temps, occasionally.
D'h en h. (D'heure en heure), every hour.
Dissoudre, dissolve.

Doigtier, a finger stall.
Douleur, pain.
Dover Poudre, Dover's Powder.
Drap d'hôpital, waterproof sheetin
Droite (à), to the right.
Ds. (Dans), in.
Enème, enema.
En se couchant, on going to bed.
En se levant, on getting up.
Ensemble, together.
Entre, between.
Etiquette, slip-label.
Etiquette avec formule, label with formula.
Flacon, bottle.
Flacon (le) ayant été agité, the bottle having been shaken.
Flatulences, flatulence.
Fomentation, fomentation.
Foulé, sprained.
Garde-vue, eye-shade.
Gargariser, gargle.
Gencives (les), the gums.
Gouttes, drops.
Hier, yesterday.
Humbergum, opium.
In caps. amyl, in cachets.
Inhalation-inhalateur, inhalation-inhaler.
Injecteur, syringe.
Injection intramusculaire, intramuscular injection.
Injection intraveineuse, intravenous injection.
Jus de citron, lemon juice.
Jusqu'à ce que, up to.
Juste avant d'aller se coucher, just before retiring to rest.
La hanche, the hip.
Lait, milk.
Main (la), the hand.
Le (or la) même, the same.
Mechoachon, Jalap.
Ne pas avaler, not to be taken.
Nuit, night.
Oeillère, eye-cup.
Ouate, Cotton wool.
Pansements, dressings.
Par degrés, by degrees.
Passe-partout, an address label.
Paupières, eye-lids.
Pendant l'effervescence, during effervescence.
Pendant que la douleur dure, while the pain lasts.
Poignée, handful.
Pour être appliqué avec la brosse, to be brushed.
Pour être appliqué avec le pinceau, to be painted.
Pour être aspiré par les narines en renflant, to be sniffed up the nostrils.

French Glossary—continued.

Pour être injecté, to be injected.
Pour l'usage partiel seulement, for local use only.
Pour placer dans l'œil, to be placed in the eye.
Pour usage extérieur, for external use.
Pr. (Pour), for.
Près de, near to.
Quand la toux est gênante, when the cough is troublesome.
Rince-bouche, mouth wash.
Sangsue, leech.
Sans, without.
Saturne, lead.
Semaine, week.
Seul. e. alone.
Si nécessaire, if necessary.
Sparadrap, adhesive plaster.
Tamiser, to sift.
Tarlatane, muslin.
Tasse, cup.

Timbre à ordonnances, Prescription Stamp.
Tous les deux jours, every other day.
Tous les matins (soirs), every morning (night).
Tous les quarts d'heure, every quarter hour.
Tous les trois jours, every third day.
Toutes les deux heures, every two hours, or every other hour.
Trouble, turbid.
Toux (la), the cough.
Un blanc d'œuf, white of an egg.
Une fois, once.
Un jaune d'œuf, yolk of an egg.
Veine, vein.
Verre à madère, wineglass.
Verrée (une), wineglass (8 cuillerées ordinaires—20 gm.)
Versez pour off.
Vessic à glace, ice-bag.

GERMAN GLOSSARY.

Abend, evening.
Abkochung, decoction.
Abwechselnd, alternately.
Ader, vein.
Alle-Stunden-Tropfen zu nehmen, so many drops every — hours.
Alle viertel Stunden, every quarter-hour.
Alle zwei Stunden, every other hour.
Allmählich, by degrees.
Anwenden, apply.
Atmen, breathing.
Auflösen, dissolve.
Augenlider, eye-lids.
Augenschirm, eye-shade.
Augenwasser, eye-wash.
Augenwimpern, eye-lashes.
Ausgenommen wenn, unless.
Ausgiessen, pour off.
Ausserlich anzuwenden, for external use.
Bahung, fomentation.
Becher, a cup.
Beim zu Bett gehen, at bedtime.
Bis auf, up to.
Blähung, flatulence.
Blutegel, leech.
Brandblase, blister.
Bursten, to be brushed.
Charpie-Bausch, tampon.
Der schmerzende Teil, the painful part.
Dasselbe, the same.
Dessertloffel, dessertspoonful.
Diese Arznei darf nicht eingenommen werden, not to be taken.
Diese Arznei darf ohne erneute schriftliche Verordnung des Arztes nicht repetiert werden, this medicine may not be repeated without written order of the physician.

Dragieren (pi'llen), to be coated (pills).
Drei mal täglich, thrice daily.
Durch die Nase einzuziehen, to be sniffed up the nostrils.
Ebenfalls, also.
Eigelb, yolk of an egg.
Eingeben, administer.
Einspritzung, injection.
Einspritzung in die Adern, intravenous injection.
Einspritzung in die Muskeln, intramuscular injection.
Einspritzung unter die Haut, subcutaneous injection.
Einzuspritzen, to be injected.
Einzutropfen, to be instilled.
Eiweiss, white of an egg.
Erbrechen, vomiting.
Erwarmen, to be warmed.
Essloffel, tablespoon.
Etikette mit Rezept, label with formula.
Eventuell, idiomatic word now very popular in German. May mean, 'if possible' or 'possibly' or 'for example.'
Flasche, bottle.
Frottieren, friction.
Für innerlichen Gebrauch, for internal use.
Gelegentlich, occasionally.
Genau, accurately.
Genugend, sufficiently.
Gestern, yesterday.
Gift, poison.
Glaskapsel oder Phiole, glass capsule or ampoule.
Glasstab, glass rod.
Gleiche Teile, equal parts.
Gargelwasser, gargle.
Gut, well.

German Glossary—continued.

Herz, heart.
 Hüfte, hip.
 Husten, cough.
 In das Auge zu bringen, to be placed in the eye.
 In der angegebenen Weise, in the manner directed.
 In der gewohnten Weise, in the usual manner.
 In gleiche Teile zu teilen, to be divided into equal parts.
 Inhalations-Apparat, inhaler.
 Jeden Abend, every evening.
 Jeden Morgen, every morning.
 Jeden zweiten Tag, every other day.
 Klystier, enema.
 Kochend, boiling.
 Kurz vor dem Schlafengehen, just before retiring to rest.
 Leder, leather.
 Löffel, spoon.
 Mazerieren, macerate.
 Messerspitze voll, as much as lies on the point of a knife.
 Morgen früh, to-morrow morning.
 Mundwasser, mouth-wash.
 Mutterzapfen, pessary.
 Nach Anweisung, as directed.
 Nach Bedarf, when required.
 Nach dem Essen, after meals.
 Nachdem man die Flasche umgeschüttelt hat, the bottle having been first shaken.
 Nach einer Stunde, at the expiration of an hour.
 Nach Gewicht, by weight.
 Nahe, near.
 Niederliegen, lying down.
 Nur auf ärztliche Anweisung abzugeben, to be given only on the medical man's direction.
 Nur für äußerlichen Gebrauch, for external use only.
 Nur für örtlichen Gebrauch, for local use only.

Ohne, without.
 Pinseln, to be painted.
 Recht, right.
 Reiben, rub.
 Reizbar, irritable.
 Schmerz, pain.
 Sofort, immediately.
 So lange der Schmerz anhält, while the pain lasts.
 Spritze, syringe.
 Stets kühl zu halten, to be kept cool.
 Streichen, spread.
 Stuhlzapfen, suppository.
 Stunde (Eine), one hour.
 Tafelchen, tablet.
 Täglich, daily.
 Topf, pot.
 Trunk, draught.
 Ueber, above.
 Uebersilbern (Pille), to be silvered (pill).
 Umschütteln, to shake (the bottle).
 Verbandwatte, absorbent wool.
 Verordnen, prescribe.
 Von Tag zu Tag, from day to day.
 Vor dem Gebrauch gut umzuschütteln, to be well shaken before use.
 Vorsicht, with care.
 Vorsichtig, cautiously.
 Während des Aufbrausens, during effervescence.
 Wenn der Husten belästigt, when the cough is troublesome.
 Woche (Eine) one week.
 Zahnfließ, the gums.
 Zahnreinigungsmittel, dentifrice.
 Zerreiben oder zerbrechen, to be crushed or broken.
 Zerstäubungs-Apparat, spray or atomiser.
 Zitronensaft, lemon juice.
 Zubereitet, prepared.
 Zu gleichen Teilen, of each equal parts.
 Zu nehmen, to take.
 Zwischen, between.

ITALIAN GLOSSARY.

A caldo, warmed.
 A essere aspirato dalle narici, to be sniffed up the nostrils.
 A frantumarsi o spezzarsi, to be crushed or broken.
 Aggiungere un cucchiaino ad un mezzo litro di acqua bollente, e fare inalazioni colla evaporazione, one teaspoonful to a "pint" of boiling water and the steam inhaled.
 Agitare la bottiglia avanti l'uso, the bottle having been first shaken.
 A gradi, by degrees.
 A idi sopra, above

A meno che, unless.
 A peso, by weight.
 Apparecchio respiratorio, respirator.
 Applicare con un pennello, to be brushed.
 Applicare la filaccia sulla ferita frequentemente, e appena asciutta ripetere di nuovo l'applicazione, Apply lint to the wound frequently, as soon as dry repeat the application again.
 Bacchetta di vetro, glass rod.
 Bollire, boiling.
 Bottiglia, bottle.

Italian Glossary—*continued.**Candela*, bougie.*Capsule o ampolle di vetro*, glass capsules or ampoules.*Ciglia*, eye-lashes.*Clistere*, Enema.*Collirio*, eye-wash*Come fu detto*, as directed.*Come fu detto avanti*, as previously directed.*Cucchiano da caffè*, dessertspoon (very few people take "tea" in Italy.)*Cucchiaio*, spoonful.*Cucchiaio da tavola*, tablespoonful.*Cuoio*, leather.*Da applicarsi dietro l'orecchio destro*, apply behind the right ear.*Da applicarsi eggermente prima di coricarsi*, to be applied lightly at bedtime.*Da applicarsi sulla eruzione cutanea*, to be applied to the eczematous rash.*Da argentarsi (pillole)*, to be silvered (pills).*Da bere*, drink.*Da instillarsi*, to be instilled.*Da ricoprirsi (pillole)*, to be coated (pills).*Da sciogliersi*, dissolve*Da somministrarsi*, to be administered.*Da strofinarsi con un panno sul cuoio cappelluto sera e mattina*, to be rubbed into the bare patch on the scalp night and morning.*Da usarsi localmente*, for local use only.*Da vicino*, near to.*Di giorno in giorno*, from day to day.*Diviso in parti uguali*, of each equal parts.*Dolore*, pain.*Domani sera*, to-morrow night.*Domattina*, to-morrow morning.*Domattina presto*, early to-morrow.*Dopo i pasti*, after meals*Dopo un'ora*, at the expiration of an hour.*Esattamente*, accurately.*Etichetta*, label*Etichetta con formula*, label with formula.*Falaccia*, lint.*Filtrare*, strain.*Fino a*, up to.*Fino a che dura il dolore*, while the pain lasts.*Fra mezzo*, between.*Frizioni*, friction.*Gargarizzare*, gargle.*Giacere*, lying down.*Giornalmente*, daily.*Giusto*, right.*Gocce*, drops (of liquid).*Idrofilo*, absorbent.*Ieri*, yesterday.*Il cuore*, the heart.*Inalazioni-inalatore*, inhalation-inhaler.*Iniezione sottocutanea*, subcutaneous injection.*Insieme*, together.*L'anca*, the hip.*La mano*, the hand.*La tosse*, the cough.*Latte*, milk.*Le gengive*, the gums.*Lo stisso*, the same.*Non piu di 4 volte al giorno*, not more than four times a day.*Ogni due ore, Un'ora si e l'altra no*, every other hour.*Ogni quarto d'ora*, every quarter of an hour.*Ogni sera*, every night.*Ogni due ore*, every two hours.*Ogni tre giorni*, every third day.*Palpebre*, eye-lids.*Pastiglie*, lozenges.*Pennellare la gola ogni giorno, una mezz'ora dopo calazione*, paint the throat every day about half an hour after breakfast.*Per iniezioni* to be injected.*Per pennellature*, to be painted.*Per pennellature alle narici due volte al giorno*, apply to the nostrils with a camel's hair brush twice a day.*Per sciacquare la bocca*, mouth-wash.*Prima di coricarsi*, just before retiring to rest.*Pure*, also.*Quando la tosse arreca disturbo*, when the cough is troublesome.*Sera*, night.*Se sara necessario*, if necessary.*Settimanalmente*, weekly.*Senza*, without.*Siringa*, syringe.*Sorso*, draught.*Spruzzatore*, spray.*Stoppaccio*, tampon*Strofinare*, rub.*Sugo di limone*, lemon juice.*Tazza*, cup.*Tre volte al giorno*, three times a day.*Tutte le mattine*, every morning.*Una goccia dentro la pupilla degli occhi una volta al giorno*, a drop into the lower lid of each eye once a day.*Una manciata*, handful.*Una settimana*, a week.*Una volta*, once.*Un bicchiere da vino*, wine-glass.*Un bianco d'uovo*, white of an egg.*Un giorno si ed un giorno no*, every other day.

Italian Glossary—continued.

In taelo d'uovo, yolk of an egg*In uovo*, an egg.*Vaporizzatore*, atomiser.*Vaso*, pot.*Veleno*, poison.*Vena*, vein.*Versare*, pour off*Vescica*, blister.*Vicino*, near.*Visiera*, eye-shade.

PORTUGUESE GLOSSARY.

A, the (feminine)*Acima*, above.*Algalia*, bougie.*Almoço*, breakfast.*Alternadamente*, alternately.*Amanhã á noite*, to-morrow night.*Amanhã pela manhã*, to-morrow morning.*A menos que*, unless.*A parte dorida*, the painful part.*A pelle de craneo, couro (cabelludo)*, scalp.*A peso*, by weight.*Applica-se suavemente na séde da dór*, to be applied gently to the painful part.*Aquecido*, warmed.*A serem cobertas (pilulas)*, to be coated (pills).*A serem prateadas (pilulas)*, to be silvered (pills).*A ser instillado*, to be instilled.*A ser pincelado*, to be brushed.*A ser pintado*, to be painted.*As gengivas*, the gums.*Atraz*, behind.*Banho para o olho*, eye-wash*Beber*, to drink.*Bem*, well.*Cabelludo*, hairy.*Calvo*, bald.*Capsulas ou ampoulas de vidro*, glass capsules or ampoules*Cautelosamente*, cautiously*Chiavna, Chicara*, cup.*Clyster*, enema.*Coár*, to strain.*Colhér cheia*, spoonful.*Colhér de chá cheia*, teaspoonful.*Colhér de doce cheia*, dessertspoonful.*Colhér de sopa cheia*, tablespoonful (soup-spoon).*Com cuidado*, cautiously, with care.*Como indicado nas instrucções*, as directed.*Com precisão*, accurately*Coração*, of the heart.*Couro*, leather.*Cuidadosamente*, carefully.*De deitar-se, á hora*, at bedtime.*De dia a dia*, from day to day.*Depois*, after.*De tres em 3 dias*, every third day.*De vez em quando*, occasionally.*Direito, lado*, right side.*Dór*, pain.*Em partes eguaes, de cada*, of each equal parts.*Emquanto durar a dór*, while pain lasts.*Entre*, between.*Erupção*, the rash.*Esfregar*, to rub.*Estender*, to stretch, extend.*Esterilisar*, sterilise.*Etiqueta com formulario*, label with formula.*Exactamente antes de retirar-se para descansar*, just before retiring.*Fios de linho, or lichino*, lint.*Flatulencia*, flatulence*Friccionar*, rub.*Fricção*, friction.*Fomentação*, fomentation:*Garganta*, the throat.*Gargarejo*, gargle.*Garrafa, or Frasco*, bottle.*Garrafa bem agitada*, the bottle well shaken.*Gemma d'un ovo*, yolk of egg.*Gotas*, drops.*Hontem*, yesterday.*Hostia*, cachet or wafer.*Inhalação - inhalador*, inhalation-inhaler.*Injecção*, injection.*Injecção intramuscular*, intramuscular injection.*Injecção intravenosa*, intravenous injection.*Injecção subcutanea (or epidermica)*, subcutaneous injection.*Irritavel*, irritable.*Lavagem de boca*, mouth-wash.*Lavagem para os olhos*, eye-wash.*Leite*, milk.*Mais*, more.*Mão cheia*, handful.*Mão*, hand.*Mesmo*, same.*Não*, not.*Noite*, night.*No meio de*, in the middle of*O*, the (masculine).*Orelha*, ear.*Para para o olho*, eye-shade.

Portuguese Glossary—continued.

Palpebras, eye-lids.
Panella, pot.
Para aspirar pela ventas, to be sniffed up the nostrils.
Para ser, to be.
Para ser injectado, to be injected.
Para ser triturado o quebrado, to be crushed or broken.
Para uso externo, for external use.
Pela manhã, in the morning.
Pellica, kid leather.
Perto (de), *junto (a)*, near (to).
Pestanas, eye-lashes.
Pó, powder.
Pulverizador, spray and atomiser.
Quadril, hip.
Refeições, meals.
Respiração, breathing.
Respirador, respirator.
Semana, uma, a week.
Seringa, syringe.
Sítio, place.
Sem, without

Sim, yes.
Sumo de Limão, lemon juice.
Taça, large cup (goblet, bowl)
Tambem, also.
Tampão, tampon.
Todos os dias, daily.
Tosse, cough.
Uma gota na pappebra inferior, a drop into the lower lid of each eye once daily.
Uma hora sim, uma não, every other hour (one hour yes, one no).
Uma vez, once.
Um dia sim outre não, every other day.
Vareta de vidro, glass rod.
Vasar, to pour off.
Veia, vein.
Veneno, poison.
Ventá, nostril.
Vesicatorio, blister.
Vez, cada, each time.

SPANISH GLOSSARY.

Acepillarse, to be brushed.
Agua para lavar laboca, mouth-wash.
Agua para lavar los ojos, eye-wash.
A la hora de acostarse, at bed-time.
Almuerzo, breakfast (lunch).
Alternativamente, alternately.
Ampollus de vidrio, glass ampoules.
A no ser que, unless.
Aparato, de inspirar, inhaler.
Apliquese suavemente al sitio del dolor, apply gently to the painful parts.
Aspiración, breathing.
Atrás, behind.
Beber, to drink.
Bien, well!
Cabella (el) del cráneo, the hair of the scalp.
Cabritilla, kid leather.
Cadera, hip.
Calentado, warmed.
Calvo, bald.
Candelilla, bougie.
Cápsulas de vidrio, glass capsules.
Cerca, near, near to.
Colar, to strain.
Comidas, meals.
Con cuidado, with care.
Con precisión, accurately.
Corazón el, the heart.
Cubrirse, to be coated (pills).
Cucharada, spoonful.
Cucharada de postre, dessertspoonful.
Cucharada de sopa, soup- or table-spoonful.
Cucharadita de t.é., teaspoonful.
Cuero, leather.
Cuidadosamente, carefully, accurately, cautiously.
De día en día, from day to day.
Derecha, right (hand).
Después, after.
De tres en tres dias, every third day.
De vez en cuando, occasionally.
Dolor, pain.
El, the (masculine).
En medio de, in the middle of.
Encías, the gums.
Encima, above.
Entre, between.
Esterilizar, sterilise.
Exactamente antes de retirarse para dormir, just before retiring.
Extender, to spread.
Frotar, rub.
Garganta, the throat.
Giro, draft.
Gotas, drops.
Hilas de lino, lint.
Inyección entrevenoso, intravenous injection.
Inyección intramuscular, intramuscular injection.
Inyección subcutaneo, subcutaneous injection.
Jeringa, syringe.
Jugo de limón, lemon juice.
La, the (feminine).
La parte que duele, the painful part.
Leche, milk.
Llegado, arrived.
Loción, eye-wash.

Spanish Glossary—continued.

mano, hand.
mañana, por la mañana, to-morrow morning.
mano llena, handful.
mañana por la noche, to-morrow night.
más, more.
mientras dura el dolor, while the pain lasts.
mismo, same.
nariz, nostril.
no, not.
noche, night.
olea, wafer.
orden (or Pedido), order.
oreja, ear.
para inspirar por las narices, to be sniffed up the nostrils.
para instilar, to be instilled.
para inyectar, to be injected.
para ser, to be.
para uso externo, for external use.
parpados, eye-lids.
partes iguales de los dos, of each equal parts.
pestañas, eye-lashes.
Píldoras (Mézclese y háganse 100 Píldoras). (*Háganse* is frequently contracted to "H"), Pills (mix and prepare 100 pills).
pintarse, to be painted.
platearse, to be silvered (pills).
polvo, powder.
por la mañana, in the morning.

Potecillo, pot.
Por peso, by weight.
Restregar, to rub.
Rociador y Pulverizador, spray and atomiser.
Romperse, to be crushed or broken.
Rótulo con fórmula, label with formula.
Sanguijuela, leech.
Según se dirige, as directed.
Semana, a week.
Sin, without.
Sitio (or lugar), place.
Tambien, also.
Tapón, tampon.
Taza, cup (drinking) or tea cup.
Todos los días, daily.
Tos, cough.
Una hora si y la otra no, every other hour.
Una gota en el párpado inferior de cada ojo, una vez al día, a drop into the lower lid of each eye once daily.
Una vez, once.
Un día si y el otro no, every other day.
Vaciar, to pour off.
Varilla de vidrio, glass rod.
Vejigatorio, blister.
Vena, vein.
Veneno, poison.
Vez una, once (one time).
Visera, eye-shade.
Yema de huevo, yolk of egg.

The title of 'Doctor' also of 'Quack,' in many languages.—I. ii. 10, 188.

INDEX & POSOLOGICAL TABLE.

THIS index supplies the name *in Latin* as far as possible and adult dose (if used internally) of most of the drugs and preparations described. The doses are based on personal experience or are culled from the best authorities.

B. P. 1914 names are printed in *italics*.

For Acids look under the word Acid.

For Salts, *vide* Latin name of the base.

The Chemicals in the Scheme for Recognition of Organic Compounds pp. 192 to 203 are *not* indexed *in extenso* in this index but those in the Corroborative Tests pp. 204 to 247 are indexed.

It has not been thought necessary to include *all* the Proprietary or Patent Medicines pp. 624 to 637.

Further, Mineral Waters and Spas 447 to 463 are *not* indexed in detail.

For Effervescent Preparations, see list under the word Effervescent.

Some items, *e.g.*, some Official Medicamenta and Pilulæ have purposely no page—*i.e.*, they are not further described in the book.

Customary CONTRACTIONS have been found necessary, *e.g.*, the following:

Acid. or Ac. = Acidus, -a, -um, etc.

All. = Alcoholic.

Ack. = Alkalinus, etc.

Av. = Average (Dose).

Caps. = Capsula, etc.

C. = cum (with).

Co. = Compositus, etc. (or compound).

Conc. = Concentratus, etc.

Eff. = Effervescens, etc.

Emplast. = Emplastrum, etc.

Emuls. = Emulsio, etc.

Expt. = Expectorant.

Extr. = Extractum, etc.

Fluidextr. = Fluidextractum.

Glycerin = Glycerinum, etc.

Glyceroph. = Glycerophosphas, etc.

HBr. = Hydrobromidum, etc.

HCl. = Hydrochloridum, etc.

Hyd. = Hydrargyrum, etc.

Hyp. = Hypodermicus, etc.

Inf. = Infusum, etc.

Inj. = Injectio, etc.

Incr. = Increased.

Linum. = Linimentum, etc.

Liq. = Liquor or Liquidus, etc.

Mag. = Magnesium, etc.

Mang. = Manganesium, etc.

Mist. = Mistura, etc.

Potass. = Potassium, etc.

Quin. = Quinina, etc.

Rad. = Radix, etc.

Rep. = Repeated.

Salicyl. = Salicylas, etc.

Sol. = Solutio, etc.

Spirit. = Spiritus, etc.

Strych. = Strychnina, etc.

Syr. = Syrupus, etc.

Tinct. = Tinctura, etc.

Ung. = Unguentum, etc. or Ointment.

Vin. = Vinum, etc.

'85 = B.P. 1885.

'98 = B.P. 1898.

'14 = B.P. 1924.

Vide also list of Abbreviations at commencement of the book.

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
A. B. C. Liniment	98	Acetyl Morphine HCl. $\frac{1}{25}$ to $\frac{1}{8}$		
„ Lotion	98	gr., 566; base, $\frac{1}{24}$ to		
„ Powder	10	$\frac{1}{12}$ gr. ...	566, 139	
Abbey's Salt	624	„ -p-amido-salol, 10 to 15 gr.	90,	
Abbreviations ...	xxv. <i>et seq.</i>			206	
Abdominal Dressings	437	„ -Salol, 15 gr. ...	82	
Abelin	163	„ tannin ...	96	
Abies Canadensis	878	Acetylation, effect of ...	256	
Aboua	863	„ process for oils ...	123	
Abrus Precatorius; Abrin	832	Acetylene ...	292	
Absinthe	832	„ Dichloride ...	292	
Acacia Catechu	848	„ Tetrachloride ...	59	
Acaciæ Cortex	832	Acetysal ...	74	
„ Gummi ...	1 & 1		Ache des Marais ...	169	
Acacia Gum Injection, Intra-			Achorion Schoenleinii ...	569	
venous	1	Acidin, 5 to 15 grains ...	43	
A.C.E. ...	285, 288		Acidol, 1 to 8 gr. ...	5	
Accessory Food Factors, ...	592, 98		Acid. Abietic ...	148	
see also Vitamins		„ Acetic., 33%, 5-15 m. ...	3 & 267	
Accouchement Sheets, Sphag-			„ Acetic. Dil., 5%, $\frac{1}{2}$ to 1 dr. ...	4	
num ...	786		„ Acetic Glaciale ...	3	
Acete de Palo (Ph. Notes)=			„ Aceto-Acetic ...	359	
Copaiba ...	624		„ Acetyl Aminohydrox-		
Acetaldehyde ...	125		phenyl. Arsonic ...	192	
Acetamide ...	6		„ Acetyl-amino-Phenyl-		
Acetanilide, 2 to 5 gr. 2 & 1, 206, 267			stibinic ...	168	
and Meth-blue tubes ...	261		„ Acetyl-Bromo-Salicylic		
Acetannin, 5 to 15 gr. ...	96		5 gr. ...	84	
Acetate d'Ammonium Dissous. ...	149		„ Acetyl-Coumar, 5 to 10 gr. ...	28	
Acetic Anhydride ...	4		„ Acetyl-Iodo-Salicylic, 5 gr. ...	83	
Acetic Ether, 45 to 60 m; 15 to			„ Acetyl-o-cresotinic ...	91	
30 m. rep. ...	110		„ Acetyl-Salicyl., 5 to 15 gr.		
Acetomorphine ...	566		74 & 14, 206, 267		
Acetone, 60-90 m. daily 832 & 206,			„ Agaric, $\frac{1}{8}$ to $\frac{1}{2}$ gr. ...	837, 206	
267			„ Allyl-iso-prop. barb. ...	821	
„ Bacillus ...	832		„ Amido-acetic, 10 to 30 gr. 4 & 95		
„ Chloroform, 1 to 5 m. ...	284		„ Amido-Succinic-Amide,		
„ in Ether ...	21		1-2 gr. ...	842	
„ Soap ...	762		„ Aminic., 2 to 10 m. ...	34	
„ in Urine ...	359		„ Amino-caproic ...	95	
Acetonitril ...	96		„ Amino-formic ...	95	
Aceto-p-amido-salol (Salophen) ...	90		„ Amino-glutaric ...	95	
Aceto-phenone, $1\frac{1}{2}$ -5 m. ...	832, 206		„ Aminophenylarsonic ...	189	
Acetopyrin, 8 to 15 gr. ...	329		„ Aminophenyl Stibinic ...	34	
Acetosal ...	74		„ Amino-propionic... ...	95	
Acet-para-phenetide ...	326		„ Amino-succinic ...	95	
Acet-phenetidid, 5-15 gr. ...	326		„ Anacardic ...	840	
Acetum ...	4		„ Aniline-arsenic ...	189	
„ Cantharidini ...	268		„ Arsanilic ...	189	
„ Cantharidis ...	268		„ Arsenic., 1/64 to 1/12 gr. ...	184,	
„ Cevadillæ ...	893		267		
„ Digitalis, Ph. Ned. ...	395		„ Arsenios., 1/64 to 1/16 gr. ...	179,	
„ Ipecac., B.P. '98, 5 to			267		
30 m. ...	—		„ Arsenoic ...	185	
„ Opil., 1 in 10, 8 m. ...	138		„ Arsinic, Arsonic ...	185	
„ Scillæ, 5-15 m. ...	885		„ Aspartic ...	95	
„ Urigineæ, 5-15 m. ...	892		„ Auro-chloric ...	219	
Acetylarsan, 1 cc. inj. ...	193		„ Azelaic ...	601	
Acetyl-Atoxyl, $\frac{1}{2}$ grain ...	191		„ Barbituric & Comps. ...	817	
„ -benzoyl-aconine ...	99		„ Benzamido-acetic ...	8	
„ Brom Salol, 5 gr. ...	89		„ Benzoic., 5 to 15 gr. 6, 2, 206,		
„ chloride ...	4		267, 492, 498		
„ Iodo-Salol, 5 gr. ...	89		„ Boricum, 5 to 15 gr. 9, 3, 267, 498		
„ -Methyl-Salicyl, 10 to			„ „ Detection, in Milk ...	3	
30 gr. ...	80		„ Boro-Salicyl. ...	10	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Acid. Bromo-Salicylic ...		14	Acid. <i>Hydrocyanic</i> . Dil., 2%.		
„ Butyl ethylbarbit. ...		821	2-6 m. 44 & 7, 26		
„ Butyric ...		54	„ „ (Scheele), 1 to 3 m. 4		
„ Cacodylic., $\frac{1}{2}$ to 2 gr. 185 & 206,		267	„ Hydrofluoric. Dil., 5-15 m.		
„ Camphoric, 10-20 gr. 264, 206,		267	et Conc. ...	83	
„ Carbamic ...		95	„ Hydrofluorsilicic... ..	77	
„ Carbazotic, $\frac{1}{4}$ to 2 gr. ...		62	„ Hydroxybutyric... ..	36	
„ <i>Carbolic.</i> , 1 to 3 gr. 13, 4, 206,		267, 362	„ Hydroxy-cinnamic ...	2	
„ „ Camph. ...		15	„ Hydroxy-succinic., 1 to 5		
„ „ Commercial ...		30	gr. ...	83	
„ „ Liq., 1 to 3 m. 15			„ Hyperosmic., $\frac{1}{64}$ gr. .	83	
„ „ Liq. et Iodum 17			„ Hypochloros. ... 44, 3, 26		
„ Carbonic ...		22	„ Hypophosphoros. ...	69	
„ Carminic ...		847	„ „ Dil., av. 8 m. ...	69	
„ Cathartic, 4 to 8 gr. ...		886	„ Iodic., 1 to 5 gr. 833, 263, 36		
„ Chaulmoogric ...		607	„ Iodo-behenic ...	52	
„ „ 'C' Injn. ...		613	„ Kinic., 4 to 8 gr. ...	72	
„ Chloracetic.(mono-, di-, tri-,) 24			„ <i>Lactic.</i> , 75%, 15 to 30 m.		
„ Cholic (Cholie) 783, 206			54 & 9, 263, 41		
„ <i>Cholic.</i> 832, 263			„ <i>Lactic</i> . Dil., 30 to 120 m. 5		
„ Chrysophanic., $\frac{1}{8}$ - $\frac{1}{2}$ gr. 294, 886			„ „ Pess. & Jelly ...	72	
„ Cinnamic, $\frac{1}{20}$ - $\frac{1}{4}$ gr. 25, 206,		263	„ Lactic Bacilli ...	57 & 11	
„ <i>Citricum</i> , 5 to 20 gr. 29, 208, 268			„ Lithic ...	36	
„ Coumaric ...		27, 208	„ Magenta ...	59	
„ <i>Cresylic.</i> , 1 to 3 m. 30, 5, 208,		263	„ Malic., 1 to 5 gr. 834, 203, 266		
„ „ Phenol in ...		5	„ Malonic ...	81	
„ Desoxycholic ...		783	„ Margolic ...	84	
„ Diacetic ...		359	„ Meconic ...	834, 200	
„ Di-allyl-barbituric, $\frac{1}{4}$ to			„ Metaphosph. ... 890, 13, 366		
4 $\frac{1}{2}$ gr. ...		821	„ Meta-vanadic. ...	89	
„ Di-chloracetic ...		24	„ Molybdic. ...	35	
„ Diethylbarbituric ...		817	„ Monochloracetic. ...	22	
„ Di-iodo-elaidic ...		523	„ Mucic ...	86	
„ Di-iodo-Taririnic ...		523	„ Naphthalene Sulphonic... 66		
„ Dineth.arsinic., $\frac{1}{4}$ to 2 gr. 185			„ <i>Nitric.</i> , 70%, 1 to 4 m.... 66		
„ Di-nitrosalicylic ...		378	„ „ Dil., 10%, 5 to 20 m. 66		
„ Dipropylbarbituric ...		820	„ Nitric Fumans ...	66	
„ Eugenol ...		857	„ Nitro-hydrochlor. Fort. . 66		
„ fast bacteria 598, 599, 601			„ Nucleic ... 281, 890, 200		
„ Ferrocyanic ...		302	„ Nucleinic. (Sol.), 15 m. 281, 890		
„ Fillicic, 6 to 15 gr. ...		423	„ Nucleotinphosphoric ...	98	
„ Fluoric ...		833	„ <i>Oleic.</i> (Caps., 7 $\frac{1}{2}$ m. 601) 600		
„ Formic., 2-10 m. 34, 268			„ Ortho-coumaric ...	27	
„ Fuchsin ...		598	„ Osmic., sol. 1%, 2 to 10 m. 833		
„ Gallic., 5 to 15 gr. 833, 208			„ Oxalic. ... 61 & 208, 266		
„ Glutaric ...		19	„ Oxy-benzoic., 5 to 20 gr. 66		
„ Glutaminic ...		95	„ Oxybutyric ...	35	
„ Glycerophosph., 5 to 10 m. 36,		6, 208	„ p. Oxyphenyl-anido-acetic		
„ Glycuronic ...		374	„ Oxyphenyl-arsonic ...	19	
„ Gynocardic, $\frac{1}{4}$ -3 gr. ...		608	„ Pelargonic ...	60	
„ Group, effect of ...		250	„ Perboric ...	15	
„ Hippuric., 5-20 gr. 8 & 208, 381			„ Perchloric ...	16	
„ <i>Hydriodic.</i> (10%), 5 to 10 m. 40			„ Phenol-sulphonic 19 & 420		
„ Hydrobrom., Conc. ...		41	„ Phenyl-acrylic., $\frac{1}{20}$ to $\frac{1}{4}$ gr. 25		
„ „ Dil., 15 to 60 m. ...		41	„ Phenylcinchoninic, 8 to		
„ Hydro-Ferro-Cyanic ...		362	15 gr. ...	317	
„ <i>Hydrochloricum</i> , 31-79%,			(See also Tabs.		
2-6m. ... 42, 268, 415			Phenoquin).		
„ Dil., 10%, 5 to 20 m. 42			„ „ Ethyl-barbituric ...	822	
			„ „ Quinolin-carbonic 317		
			„ <i>Phosphor. Conc.</i> , 66-80%,		
			1 to 4 m. 61 & 13		
			„ „ Dil., 10%, 5 to 20 m. 62		

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Acid. Phospho-Molybdic. ...		204	Aconitinæ HBr.HCl., Nit. 1/600		
„ Phospho-tungstic ...		204	gr. hyp. ...	100	
„ Phthalic ...		9	„ Oleat., 1 in 50 ...	100	
„ Picramic ...		378	Aconitum Laciniatum ...	835	
„ Picric., $\frac{1}{4}$ to 2 gr. 62 & 13, 268,		268	Acorn (<i>vide</i> Aesculus) ...	835	
„ Propylbarbituric ...		820	Acqua del Pagliari ...	139	
„ Prussic. Dil., 2-5 m. ...		44	Acridine Compounds ...	300 & 210	
„ Pyrogallie. 64 & 208, 268		268	Acridavine ...	300, 210	
„ „ Oxydat. ...		64	„ Antiseptic Power	301 & 265, 269	
„ Pyrolignos. Crudum, and			„ Emulsion ...	304	
Rectif. ...		4	„ in Gonorrhœa ...	303, 305	
„ Pyrophosph. ...		13	„ in Pyogenic Infec-		
„ Pyrotartaric ...		19	tions ...	302	
„ Quillaic ...		881	„ Intrav. Injection ...	303	
„ Quinic., 4 to 8 gr. ...		726	„ Literature ...	304	
„ Quinoline-carboxylic ...		317	„ Neutral (Euflavine) ...	305	
„ Ricinoleic. ...		620	„ Patents and Mfre. ...	300	
„ Rosolic ...		418	„ Prophylactic Use ...	303	
„ Salicylic., 5 to 20 gr. 65, 13,		13,	„ Soap Paste ...	304	
208, 268; in food 434, 498		434, 498	„ Starch Poultices ...	305	
„ Salicyl-sulphonic. 361, 363		361, 363	„ Strengths for Use ...	302	
„ Santonic and Santoninic 760		760	„ Subcut. Injection ...	303	
„ Sclerotic., $\frac{1}{4}$ - $\frac{3}{4}$ gr. 408, 208		408, 208	„ Therap. Coefft. ...	302	
„ Silicic ...		778	„ Therapeutic Uses 301, 304		
„ Sozolic. ...		19	„ Wounds, Suppura-		
„ Stearic. ...		91, 208	ting, and Prophyl-		
„ Succinic., 5 to 10 gr. 835, 208		835, 208	axis ...	302	
„ Sulphanilic., 5 to 10 gr. 308		308	Acrinyl Sulpho-Cyanide ...	160	
„ Sulphocarboic ...		19	Acrosyl ...	32	
„ Sulpho-vanadic ...		14	Actæa Racemosa ...	851	
„ Sulphuric., 95%, 1 to 2			Actinium. ...	328, 329	
m. 92 & 17, 269		269	Actinomycosis ...	713 & 503	
„ „ Aromat., 5 to			Activated Alkaloids ...	132	
20 m. ...		92	„ Charcoal ...	846	
„ Sulphuric. Dil., 10%, 5-			Activators ...	77	
20 m. ...		92	Activin ...	9	
„ „ Fumans. ...		93	Acton on Quinidine, etc. ...	719	
„ Sulphuros., 30-60 m. 93, 18, 269		93, 18, 269	Adalin, sedative, 5 to 10 gr.,		
492, 498		492, 498	hyp., 10 to 15 gr. ...	820	
„ Sulphone-dichloramino-			„ Characterisation ...	210	
benzoic (Halazone) ...		54	Adams' Mercurial Injection ...	455	
„ Tables ...		249	Adamson's Ringworm Ointment 1093		
„ Tannic., 5 to 10 gr. 94, 13		94, 13	Addiction, Cocaine ...	332	
205, 210, 269		205, 210, 269	„ Heroin ...	567	
„ Tartaric., 5-20 gr. 96, 18, 210,		96, 18, 210,	(See also Drug Addiction.)		
269		269	Adepsine Muls ...	570	
„ Telluric ...		607	Adeps and Adeps Benz. ...	835	
„ Thyminic, 5 to 10 gr. ...		984	„ Induratus ...	835	
„ Trichloracetic 25 & 269, 364		25 & 269, 364	„ Lotus ...	835	
„ Trichlorphenic ...		21	„ Suillus ...	835	
„ Trinitrophenic ...		62	Adeps Lanæ and Hydros. ...	100	
„ Uricum and Estimation 329		329	Adnephria ...	976	
„ Valerianic, 1-5 m. 825, 210		825, 210	Adonis Vernalis (Adonidin, $\frac{1}{4}$ to		
„ Vanadic., meta. ...		892	$\frac{1}{4}$ gr.), 3 to 6 gr. ...	835	
Acids, Action of on Metals ...		177	Adonite ...	835 & 607	
„ Fatty Unsaturated 601, 616, 619		601, 616, 619	Adormidera, F.E.=Papaver ...	—	
„ Mineral, Sale of ...		1000	Adrenalin, 976; Cathetic Lub.		
Acne, Bacteriology of ...		503	982; Dilutions, 978; Chlor.		
„ Lotion ...		830, 881	Sol., 10 to 30 m., 977; in		
„ Vaccine ...		905	Chlorof. Anæsthesia, 978;		
Acocanthera ...		791, 835	Idiosyncrasy, 979; Inhalant,		
Aconite Napellus Leaves, Root			981; Intracardiac Injection,		
and Preps. ...		97 & 19	980; Lamellæ, 981; Oint-		
Aconitina, 1/600-1/200 gr. 99 & 20, 210		99 & 20, 210	ment, 982 References, 978		

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Solution, 977; Sterules, 981;			Ajenjo, F.E.= Absinthe.		
Styptic Gelatin, 981; Syn-			Ajowan	8100	
thesis, 977; Suppos., 981;			Alabone's Treatment	8666	
Tablets, 1/65 and 1/200 gr.,			Albargin... ..	1777	
981; Tests, 170, 210; Uses	978		Alanine	955	
As test in eye work.—W.M.			Alastrim... ..	9555	
Beaumont, B.M.J., June 30/28,	1104.		Albumin Vegetable	591	
Adrenine	976		„ Ovi siccum	5833	
Adrenol Solution	981		„ Sanguinis	5833	
Adsorption	104		„ Tannicum, P. Jap. 95,	2100	
Ædes aegypti	612		„ Tests	361—364	
Advita	102		„ Water	5833	
Ægle Marmelos... ..	844		Albuminuria	361—364	
Acrugo	389		Albumoses	364	
Aeroplane Dope	443		Alcaptonuria	3800	
Aesculin, Aesculus	835, 210		Alchemilla Arvensis	8337	
Æther, 45 to 60 m.; or 15 to 30			Alcohol, Absolute, 113, 23, 269;		
m. rep., 101; Impurities, 20;			and Oxygen, 635; Allyl, 118;		
with Atropine, 105; in saline	105		Amylic, 119; Caprylic, 385;		
Æther Aceticus, 45 to 60 m.; or			Diluted, 113 et seq., see also		
15 to 30 m. rep.	110		Tables 22—25; for burns,		
Æther Camphoratus	263		117; Duty, Current, 114;		
„ Copal	869		Duty free, 122; Injections,		
„ Dimethyl	110		116; Isopropyl, 122, 23, 289;		
„ Methylat.	102		Mastichi, 869; Methylic, 30 to		
„ Nit. Spirit	109		60 m., 119, 24, 210; Methy-		
„ Petrolei	660		lated, 120; Prohibition, 117;		
„ pro narcosi	102		Propyl n., 124; Sandarachi	6977	
„ Purificatus, 10 to 30 m.	102		Alcohol, Industrial	120, 1211	
„ Purissimus	102		Alcohol Camphré	2633	
„ Rectif.	102		Alcoholism	277	
„ Spirit Camph.	383		„ Gold in, 371, 561, 10360		
„ Sulphuricus	101		Alcoolat Mélisse Comp., 20 to		
Ætherolea in P. Svec.= Olea			25 drops	8700	
Essentialia q.v.	—		„ de Fioraventi.	7022	
Æthocaine	346		Alcoolature d'aconit	977	
Æthusa Cynapium	836		Alcoolatures Stabilisées, Valé-		
Æthyl Bromidum	836, 210		riane and Aesculus... ..	824, 8366	
„ Chloridum	110, 210		Alcresta Tabs.	5355	
„ Iodidum	112, 210, 271		Aldehyde group, effect of	2566	
Afridol Violet	315		Aldehydum Absol. et Dil. 125,	2100	
Agar, 'Flaked' Almond, Van-			„ Formicum	126 & 239	
illa, Raspberry, etc.,			Alder Buckthorn	8588	
flavoured 1 dr.	836		Ale	266	
Agar and Blood Agar Media	617, 619		Alembroth Preps.	4722	
Agaricus Albus, 10 to 30 gr. ...	836		Alepol	6111	
Agaricin, $\frac{1}{2}$ to $\frac{1}{2}$ gr.	837		Aletris Cordial, $\frac{1}{2}$ to 1 dr. ...	8377	
Agaric, Surgeon's	838		Aletris Farinosa	8377	
Agave Mexicana	879		Algæ in ponds	700	
Agglutinating Sera, Standard	604		„ „ water	441	
Agglutinins	896, 995		Alginoïd Iron, 2 to 15 gr. ...	8377	
Agmel, $\frac{1}{2}$ oz.	879		Algiron, 2 to 15 gr.	8377	
Agomensine Tabs., 1 to 3	960		Algodon, F.E.= Gossypium.		
Agotan, 8 to 15 gr	317		Alibour Water	3900	
Agricultural Poisons 178, 997,	1000		Alizarin Indicator	4133	
Agrimony	837		Alkagen Tabs., 1 to 3	5466	
Agropyrum	837		Alkali Bismuthyl Tartrates	2383	
Aguamiel	879		Alkali Blue	2	
Agurin, 10 to 15 gr.	805		Alkaline Meth. Blue	598	
Air, Iodine in	430		Alkaloids, Activated	132	
„ Liquid	636 & 141		„ Detection of	204	
„ Testing for Iodine	430		„ Passage thro' system	252	
„ „ for Acetone... ..	360		„ Titration	192	
Aix-la-Chapelle Treatment ...	713		Alkaloidal Bases	132	
Alrol, Alroform, Airogen	236		„ Notes	132, 30	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Alkaloidal Oils	621	Alumini Trisulph.	...	139
„ Mercuric Iodides	136	Aluminium Bronze	48
„ Periodides	135	Aluminium, soldering of	142
„ Reagents	204	Aluminium vessels	142
Alkanet	840	Alumnole	142
Alkannin	840	Alypin and Nitras $\frac{1}{20}$ to $\frac{1}{2}$ gr.	345,	69, 221
Alkaptonuria	330	Amaas	955
Alkarsin	185	Amadou	838
Alkyl groups, effect	254	Amalgam Hg.	457
Allantoin and Dressing	889,	210,	Amani Institute	296
Allen's Dietetic Treatment	1052	Amanita Phalloides, <i>see</i> Fungi		
Allen's Fehling Test	375	Antidote Chapter.		
Allergy	666	Amanita Muscaria	837
Allium, $\frac{1}{2}$ to 2 dr.	837	Amapola, F.E.=Flos Papaveris		
„ Ceba	838	Amatol	61
„ Porrium	838	Amber, Amber Oil	889
Allocain Lumiere, 349; S.	350	Ambergris	839
Allonal, 1 to 2 Tabs.	821	Amboceptors	897 & 602
Alloxan	210, 328	Ambrein...	839
Allspice	877	Ambrine...	654
Allyl Alcohol	118,	764	American Indian Hemp	170
„ Isopropyl malonylurea...	821	Ametox	94
„ Isosulphocyanide			Amido-acet.-p-phenetidin HCl.		327
	764 &	160	Amido-acids	4, 5 & 95
„ phenyl cinchoninate	319	Amido-phenol (<i>p.</i>)	296
„ Sulphide, $\frac{1}{2}$ to 2 m. ...	837,	269	Amido-Succinic Acid Amide	842
„ Sulphocarbamide	764	Amidol, 296; Hair Dye	34
„ Thio-urea	764	Amidopyrin, 5 to 8 gr., and		
Allylene	838	Comps.	330
Almata	591	„ allyl-prop-barbiturate	821
Almen's Test	377	„ Diethyl Barbiturate and	...	330
Almizcle, F.E.=Moschus.			„ Sulphamino-benzoic		
Almond, Bitter	151	Acid	331
„ Chinese	841	Amines	202
Alnus Glutinosa	838	Amino Acids ...	4, 5 & 95,	203
Alocol Tabs.	141	„ Arseno-phenol	194
Aloe, 2 to 5 gr. 137, 31, 212; Cape	137,	212	„ -azo-benzene-azo β naph-		
			thol	326
Aloin, $\frac{1}{2}$ to 2 gr. ($\frac{1}{4}$ gr.=1 gr.			„ -azo-Toluene	313
ext.)	138, 31,	„ Benzoic Ethyl Ester	350
Alopon, $\frac{1}{2}$ to $\frac{1}{4}$ gr.	632	Aminobenz.	345
Alpha Naphthol, 2 to 5 gr.	571	Aminoform, 5 to 15 gr.	450
Alsol	140	Amino group, effect of	251
Alstonia	838	Aminophenol (<i>p.</i>)	296
Althæa 838; Althein, 1 to 2 gr.	842		Amino-Phenylarsonic Toluene		
Alum. Ammon. <i>vel</i> Potass., 5 to			Sulphonate	209
10 gr.	139	Amino-Stiburea	168
Alumen, U.S.=Potash Alum...	139	Aminothiobenzene	799
Alum, Box	434	Amiodoxyl Benzoate	90
„ Carmine	847	Ammonia, Cloudy, Household	...	149
„ <i>Exsicc.</i>	139	Ammoniated Quinine, $\frac{1}{2}$ to 1 dr.	...	738
„ Iron, 3 to 10 gr.	421	Ammonia Liquida ...	48,	269
„ Points	139	Ammoniacum, 5 to 15 gr.	—
„ Ust.	139	Ammon. Acetas, 10 to 30 gr....	...	149
Aluminii Acetas Neut. and Basic	140		„ Benzoas, 5 to 15 gr....	...	7
„ Aceto-Tart.	140	„ Bicarb., 3 to 10 gr....	...	145
„ Chloras ...	141,	269	„ Bromid., 5 to 30 gr.		
„ Chlor., 2 to 4 gr.	141		144 &	50
„ Formas	141	„ Carb., 3 to 10 gr.	145,	31
„ Hydroxidum 141, 365, 369			„ Carbamas	145
„ Naphthol-Sulphonas	142		„ Chlorid., 5 to 20 gr....	...	145
„ Silicas ...	142, 39,	374	„ Citras, 30 to 60 gr.	...	150
„ Sulphas	139	„ Cupri Sulph.	390
„ Tannas.	95	„ Cyanas	816

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE	PAGE
Ammon.	Fluorid., 1/24 to 1/8 gr.	833	Anæsthesia by Cocaine Infiltra-		
"	Hippuras, 5 to 10 gr.	8	tion		344
"	Hypophosph., 1 to 6 gr.	690	Anæsthesia by Cocaine Lumbar		
"	Iodidum, av. 5 gr....	146	puncture		344
"	Mercuric Chloride ...	472	Anæsthesia with Oxygen and		
"	Molybdate ...	73, 204	Gas, 147; Ether, Oil of		
"	Nitras ...	146	Orange in, 105; Ether and		
"	Ortho-iodoxybenzoate	90	Saline, 105; Intramuscular		
"	Persulphas ...	161, 276	106; Intratracheal, 106;		
"	Phosphas, 5 to 20 gr.	—	Pharyngeal, 106; Oral, 108;		
"	Picras, 1/8 to 1/8 gr. ...	63, 13	Rectal		100
"	Rhodanid (Sulpho-		Anæsthesia by Eucaine Infiltra-		
"	cyanid.)	31	tion		344
"	Salicylas, 5 to 30 gr.	67	Anæsthesia by Novocain, Intra-		
"	Sod. Phosph. ...	777	arterial		344
"	Succinas, 2 to 5 gr.	835	Anæsthesia by Novocain-Sup-		
"	Sulphas 147, Synthetic	53	rarenin Infiltration ...		344
"	Sulpho-Molybdate	73, 204	Anæsthesia by Scopolamine		
"	Sulpho-Ichthyolas, 10		Morphine		499
"	to 30 gr. daily ...	503	Anæsthesia, Oil Ether ...		100
"	Tartras ...	150	Anæsthesia by Synergism in		
"	Valer., 1 to 8 gr. ...	147	labour (Gwathmey) ...		100
Ammonal	61	Anæsthesia by Quinine ...		733
Amœba buccalis	530, 927	Anæsthesia Spinal by Mag.		
" coli	541	Sulph....		544
" histolytica,	526 & 541	Anæsthesia by Tropacocaine...		344
Amœbic Dysentery, Emetine in			Anæsthesia by Stovaine	351 et seq.	
	526, 533,	537	Anæsthesia by Urea Quinine ...		733
Ampere, <i>see</i> Iontophoresis	...	282	Anæsthesine, 3 to 8 gr.	350, 211	
Amphotropin, 8 to 12 gr.	...	453	Anæsthetic, Dental		338
Amydracaine	345	Anæsthetics General, Local—		
<i>Amygdala Amara; Dulcis</i>	151, 152,	31	<i>v.</i> Therap. Index.		
Amygdalin	151	" Pharmacology of	...	66
Amyl Acetate	33	Anæsthol		288
" Alcohol, 119, 32; Tertiary	839		Analgésine, 5 to 15 gr.	...	322
" Butyrate	28		Analysis of Patent Medicines	...	622
" Colloid	360		" of Prescriptions ...		633
" Hydride	660		Analytical Memoranda <i>re</i> Urine,		
" Nitrate	33		etc.		353
" Nitris, 1-5 m., Hyp. 1/2-1			Anamirta Paniculata	...	877
m. by mouth, 2-5 m.			Ananassa Sativa	...	846
inhaled	152 & 32,	212	Anaphylaxis, <i>see</i> Protein		
" Nitrite Sterules, 1, 2, 3,			Therapy <i>and</i>	603
4, 5, 6, 10 m.	...	153	Anarcotine, 1 to 3 gr.	...	573
" Nitrite and Pilocarpine			Anasarcin Tablets	...	888
Hair Lotion	...	157	Anchusa	...	840
" Phthalate	442		Anderson's Ointment	...	233
" Salicyl.	73		Andira Araroba	...	293
" Valerianate, 2-5 m.	826, 212		Andrewes' Test...	...	388
Amylase	637, 76	Anesthone, 350; Cream and		
Amylene	839	Tape... ..		350
Amylene-Chloral, 5 to 50 m.	839, 212		Anethol		840
Amyleni Hydras (Caps. 10 m.),			Anethum	...	840
30 to 80 m., 839, 212; Carbam.	839		Angier's Tablets	...	624
Amylocaine	350	Angina	...	153
Amylopsin	637	Angiolymphæ	...	883
<i>Amylum</i>	839	Angström Units	...	316
Amysal	73		Angostura	...	853
Anabol, Anabolin	963	Anhalonium	...	840
Anacardium	839	Aniline Dyes	300 et seq. in food	495
Anacyclus Pyrethrum	...	880	Aniline (Aniline Oil)	307, 212	
Anæmia, Liver Diet 962; <i>v.</i> also			Gentian Violet, 614; Red,		
Therap. Ind.			320; Sulphate, 1/2-3 gr.	307	
Anæsthesia by Chloroform	...	285	Animal Organotherapy	957 & 169	
" " Cocaine Ionisation	...	285	" Membrane	...	958

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Aniodol, 130; Anions Anode		279	Antimony Butter	...	33
Anise Fruit and Preps.	...	840	" Colloidal	...	369, 378
" Oil	...	840	" Comps., Organic		
Ankylostomiasis 274, 422, 614,			161 <i>et seq.</i>	...	34
810, 850, 876, 1032 &		504	" Crocus	...	158
Anatto and substitute	...	498	" Metal	...	157, 168, 33
Anoci-Association	...	499	" Poisoning	...	33
Anodyne Colloid	...	360	" Thioglycocollamide	...	169
" Tincture	...	631	" Toxicology	...	33
Anojheles <i>var.</i>	748 <i>et seq.</i> &	558	" Vitamin Tests	...	99
Anserine Mulls	...	570	Antinosin	...	679
" Thiosinamin	...	765	Anti-pneumo Serum	...	925
Antexema	...	625	Antiphlogistine	...	431
Anthelmintics, 422, 424; <i>see</i>			Antipyretics	...	299, 1061
also Worms, Therap. Ind.			Antipyrine, 5 to 15 gr.	...	327
and 504			Antipyrine, Acetylsalicyl, 8 to		
<i>Anthemidis Flores</i>	...	840	15 gr.	...	329
<i>Anthemis Cotula.</i>	...	841	" Caffeno-cit., 8 to		
<i>Anthion</i>	...	161	15 gr.	...	252
<i>Anthoxanthum Odorat.</i>	...	841	" Salicyl., 15-30 gr.	...	329
Anthraquinone bodies...	279, 886, 31		Antirrhinum	...	837
Anthrarobin	...	309, 212	Antiseptic Cr��d��	...	176
Anthrax Serum	...	905	" Inhalation	...	385, 386
" Bacillus	...	505	Antiseptics, for storing Instru-		
" Infn. Shaving Brushes	906		ments—Thymol		
" Treatment of Wool...	906		Disinfectant.		
Antibacterial sera	896 <i>et seq.</i>		" Glycerin and Car-		
Antibodies	...	896	bolised Glycerin	...	273
Anticatarrh Salts	...	18	" Table of	262 <i>et seq.</i>	
Anti-cholera Vaccine	...	913	" Iontophoresis	...	285
Anti-colon B. Serum	...	914	" Mercurome	...	479
Antidote Cocoon	...	857	" Oils Essential as		
Antidotes, <i>see</i> The Poison in			600 &	126	
question and...	...	1100	" Specificity of	...	265
Antidotum Arsenici, � oz. every			See also Disinfectants.		
5 or 10 minutes	...	180	Antisera, 899; Prepn. of	...	899
Anti-Dysentery Serum	...	917	Anti-smoking Gum	...	880
" Vaccine	...	918	Anti Strepto-Serum	...	928
Antifat	...	624	" -Vaccine	...	929
Antifebrin, 2 to 5 gr.	...	2	Antitoxins	...	896
Antiformin	...	600	See also Disease or Organism		
Anti-gas-gangrene Serum (W.)			and Vaccines.		
10 Cc.			Antityphoid Inoculation	...	948
<i>See Peritonitis and Tox��mia,</i>			" Tabs.	...	779
<i>Therap Ind.</i>			Antivenene	...	571
Antigen	...	896	Antivenerea! prophylaxis,		
Antilusin, Antilytic Serum	...	973	458, 461,	474	
Antimeningococcus Serum	...	912	Antivirus	...	898
Antim. Arsenas, 1/100 gr. inc.	157		Antuitrin	...	968
" Chloridum	...	33	Anturic Bath Salts	...	625
" Fur dermatitis	...	33	Apathy's Syrup	...	616
" Nig. Purif.	...	158	Aperfine, 2 to 4 dr.	...	657
" Oxidum, 1 to 2 gr.	...	158	" Liquid, 2 to 4 dr.	...	657
" Injections	...	158	Aperient Water	...	781
" Pentasulphid.	...	158	Aperitive Elixir, � to 1 dr.	...	138
" Pot. Tart.	161, 33,	212	Aperol	...	657
	269		Aphrodine, <i>cf.</i> Yohimbine.		
" in C. S. Fever	...	912	Aphthous Fever	...	486
" Sodii Tart., � gr. intrav.			Apiol Liq. (& Cryst.), 3 to 6 m.,		
increased	...	166	169, 212; and Ergotin Caps.,		
Antim. Sulphuratum, 1 to 2 gr.	157,		169; White	...	169
	33		Apiolin	...	169
Antimon. Tartarat.			Apis Mellifica	...	841
{Diaphoret, 1/25 to 1/8 gr.}	161, 33		Apium Graveolens	...	169
{Emetic, � to 1 gr. ...}			" Petroselinum	...	169

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Aplopappus	863	Areca, Arecoline and HBr.	841,	251
Apocodein, HCl., 1/10 to 1 gr.	357,	214	Argein	177
Apocynamarin	170	Argenti Acetas	173
Apocynum	170	,, Chloridum	173
Apomorphinæ HCl., $\frac{1}{16}$ to $\frac{1}{4}$ gr.	,, Citras (Itrol)	176
by mouth; 1-20 to 1-10 gr.	,, Cyanidum $\frac{1}{4}$ to $\frac{1}{20}$ gr.	...	173
hypoderm.	170, 139,	214	,, Fluoridum	176
Aponal, 15 to 30 gr.	839	,, Iodid. Recent	173
Apophesine	353, 69	,, Lactas (Actol), $\frac{1}{4}$ gr.	176,	214
Appendicitis	1033,	505	,, Nitras, $\frac{1}{4}$ to $\frac{1}{2}$ gr.	174 &	269
Apple Essence	826	,, Nitras, Fusus	175
Applicatio Acriflavine	304	,, Nitras, Indurat. et
Apricot Oil	151,	31	,, Mitigat.	175
Aq. Ammon. Fortior, U.S.	...	148	,, Nucleinas	281
,, Ammon., U.S., 15 m.	...	148	,, Oleas ($\frac{1}{4}$ to $\frac{1}{2}$ gr.?)	604
,, Amygdalæ Amaræ	152	,, Oxidum, $\frac{1}{4}$ to 2 gr.	175
,, Anethi, $\frac{1}{2}$ to 2 oz.	—	,, Potass. Iodid.	173
,, Anisi, $\frac{1}{2}$ to 1 oz.	840	,, Proteinæ	177,	214
,, Aurant. Flor., $\frac{1}{2}$ to 2 dr.	842,	46	Argent. Hair Dye	34
,, Bromoformi, 1 to 4 oz.	...	246	Argentide	173
,, Camphoræ (Conc. 172), $\frac{1}{2}$ to	Argento-Proteinum Mite, 176;
2 oz.	262	Fort	177
,, Carminativa	852	Argentum Colloidale, $\frac{1}{2}$ to 2 gr.	176,	34
,, Carui, $\frac{1}{2}$ to 2 oz.	—	(See also Colloids).
,, Chlorof., $\frac{1}{2}$ to 2 oz.	289	,, Collosol	377
,, Cinnamomi Conc.	172	,, Crédé	176
,, Coloniensis v. Eau de Cologne.	,, Proteinic	177
,, Creosoti, 2 dr.	384	Argon	636
,, Destillata	435	Argyrol	176, 214
,, Dissocians, 2½ oz.	781	Arhovine (Caps.), 4 m....	...	812
,, Fœniculi, $\frac{1}{2}$ to 2 oz.	857	Aristochin (Aristoquinine), 1 to
,, Formalinata.	127	10 gr.	742
,, Hæmostatic (Alum)	139	Aristol, 509; Aristolochia	886
,, Hamamelidis	448	Arithmetical Memoranda (V.I.)	xxxiii.	...
,, Hydrogenii Dioxidii, $\frac{1}{2}$ to 2 dr.	493	...	Armoraciæ Radix	852
,, Laurocerasi, $\frac{1}{2}$ to 2 dr.	151,	32	Arneth Index	397
,, Mellis	118	Arnica Flores	841
,, Menthæ Piperitæ, $\frac{1}{2}$ to 2 oz.	—	...	Aromadendral	130
,, Menthæ Viridis, $\frac{1}{2}$ to 2 oz.	—	...	Aromatic Confection	629
,, Menthol	557	Aromatic Elixir, $\frac{1}{2}$ to 2 dr.	...	401
,, Naphæ	842	Arrhénal, 2/5 to 3 gr.	188, 38,	214
,, Picis, 5 to 10 oz....	300,	703	Arrow Poisons	853, 875
,, Pimentæ, B.P. '98, $\frac{1}{2}$ -2 oz.	—	...	Arrowroot	814, 869
,, Pruni Macroph.	152	Arsacetin, $\frac{1}{2}$ gr.	191, 39
,, Psychotis	810	Arsamin, $\frac{1}{2}$ to 3 gr.	189, 38,	214, 270
,, Regia	60	,, Paste	190
,, Rosæ, 1 to 2 oz.	—	Arsenic Compounds Organic
,, Sambuci	883	185 & 38,	257	...
,, Saturnina = Liq. Plumbi	,, Act	997, 1000
Subac. Dil.	,, Anilide	189
,, Sedativa	263	,, Antidote, $\frac{1}{2}$ oz. every 5
,, Zeozoni	835	mins.	180
Aquæ Concentratæ	172	,, Chlorid. Vitam. Test...	...	99
Aquaperia Water	448	,, Colloidal	369
Arabic Glossary	640	,, Eating	35
Arabinose for <i>B. typhosus</i>	...	607	,, Horticultural Use
Arachis	841	178, 997, 1000
Araroba	294,	295	,, Tests	35 et. seq.	...
Arbor Vitæ	892	,, Wood Preservers	35
Arbutin, 5 to 15 gr. ...	841,	214	Arsenic, White, 1/60 to 1/15 gr.	...	179
Archil	92	Arsenical Cigarettes	185
Arctium Lappa	866	,, Fibre, 182; Paste	182
Arctostaphylos Uva Ursi	...	841	Arsenii Bromidum, 1/60 to 1/12
			gr.	181

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
<i>Arsenii Iodidum</i> , 1/20 to 1/5 gr.		182	Arsenobenzol Wassermann's Re-		
" <i>Trioxidum</i> ...		179	action, Effect on ...		43
Arsenious Wool ...		182	Arsenobillon ...		194
Arsenium, 178, 35; dimethyl ...		185	Arsenoic Bodies ...		185
Arsenobenzene, 0.1 to 0.4 Gm.		194, 214	Arsenphenolamine ...		194
Arsenobenzol, 0.1 to 0.4 Gm.		194, 214	Arsphenamin ...		194
" Assay ...		40 <i>et seq.</i>	Arsylbismol ...		193
" Uses in syphilis ...		196	Artemisia Maritima <i>et var.</i>		759
" Hereditary syphilis, 206;			" Absinth. ...		832
para-syphilis ...		196, 201	Arterial Tension ...		579
" Other diseases ...		196	Arthritis, Rheumatoid, 675, 928;		
" After effects ...		201	<i>B. Coli</i> in, 915; <i>see also</i>		
" Arsenic Retention ...		42	Protein Therap. and Therap.		
" Chemistry of Injns. ...		198, 42	Index.		
" Chemotherapeutic Index ...		195	Arthrytin ...		90
" Commercial Samples ...		195	Artificial Cream Act ...		486
" Contraindications ...		202	" " " First case under		486
" Deaths under ...		202	Artificial pneumothorax ...		636
" Doses ...		197 <i>et seq.</i>	Artificial Respiration ...		146
" Doses, Interval between ...		199	" Silk ...		439
" Dose, Maximum ...		200	Arum Maculatum ...		841
" Dysentery, for ...		536	Arylarsonates ...		185, 38
" Estimation of Arsenic ...		38	<i>Asafetida</i> , 5 to 15 gr.		842
" Examination for Spiro-			Asaprol ...		362
chetes ...		44	Asbestos... ..		144
" Glucose with ...		200, 202	Ascaridole ...		850
" Injection Methods—			Ascaris, 759, 505 (and <i>see</i>		
Intramuscular ...		198	Worms, Therap. Index).		
Subcutaneous ...		197	Asclepias ...		842
Intravenous ...		197	Aseptafilm ...		435
" Jaundice ...		202	Aseptic Wax ...		849
" Local Anæsthetics in ...		200	Aseptol ...		19
" Local Use ...		200	Asparagin, 1 to 2 gr....		842, 214
" Manufacture ...		195	Aspergillus ...		666, 498
" Mercury, combined use... ..		199	Asphyxiating Gas, poisoning		
" Neo, 0.3 to 0.45 Gm. ...		204	by, <i>see</i> Chlorine ...		1101
" Neurosyphilis ...		201	Aspidium (and oleo-resin) ...		422
" Oily Suspensions of ...		198	Aspidospermine ...		880
" Patents, Details of ...		194	Aspidinofilicinum Oleo-		
" Preparation of Injn. ...		198	Solutum ...		424
" Recognition ...		43	Aspirgran ...		74
" Rectal Use ...		199	Aspirin, 5 to 15 gr. ...		74, 267
" Serum of patient used ...		200	" Absorption of ..		15
" Silver, 0.1 Gm. ...		203	" Hydrolysis of and		
" Sodium Formaldehyde			Purity of ...		14, 15, 16
Sulphoxylate, 0.3 to			" Potass. Cit. with ...		16
0.45 Gm. ...		204	Aspirinoids ...		74
" Standard preparation ...		194	Aspriodine, 5 gr. ...		83, 214, 270
" Suppositories ...		199	" Tablets, 5 gr. ...		84
" as a test for Syphilis ...		44	" Salts ...		84
" Tests Physiological			Aspro ...		74
194 & 40, 41			Asteriastigma ...		605
" Therapeutic Subs. Act .		194	Asthma Cigarettes ...		717
" Therap. Tests ...		41	" Cure, Potter's 717;		
" Trade Marks ...		194	(Tucker's) ...		636
" Toxic effects and Treat-			" Fluid Comp. ...		213
ment ...		201, 202	" Peptone Injn. for ...		668
" " Sod. Thiosulph. for		202	" Powders ...		717
<i>See also</i> 94.			" Sensitisation ...		664 <i>et seq.</i>
" Toxicity Tests ...		40	" Skin Tests ...		664 <i>et seq.</i>
" Uses ...		196	" Spray ...		213
" Warnings and contra-			" Vaccine ...		906
indications ...		202	" Atmospheric Pollution		140
" War Office Method ...		199	Atomic Disintegration... ..		326
			Atomic Weights ...		xxxi.

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Atophan, 8 to 15 gr. ...		317	B.M.R. ...		992
Atophanyl ...		318	Bacelli's Mixture, $\frac{1}{2}$ to 1 oz. ...		181
Atoquinol ...		319	" Tetanus Method ...		931
Atoxyl, $\frac{3}{4}$ to 3 gr. ...		189	Bacilluria. <i>See</i> Bac. Coli Vac-		
Atrinal ...		632	cine & 533, 534		
<i>Atropa Belladonna</i> ...		210, 222	Bacillus Abortus ...		559
Atrophic rhinitis, <i>see</i> Therap.			" Ac. Butyrici ...		487
Index.			" " Lactici ...		57, 10
<i>Atropina</i> , 1/200 to 1/100 or 1/16			" Acetone. ...		832
gr. ...		210, 214	" Acne ...	905 &	503
Atropine Steriloids ...		134	" Acidophilus ...		59, 12
Atropinæ Methyl-Bromid., 1/64			" Aerogenes Caps. ...	12,	546
to 1/32 gr. ...		216, 214	" Aertrycke ...	509, 550,	609
" Oleatum ...		215	" Anthracis ...	905 &	505
" Salicyl, 1/60 gr. ...		213	" Asthenogenes ...		507
" Sulph., 1/200 to 1/100			" Bordet. ...	956 &	612
or 1/16 gr. ...		213	" 'Bottle' ...	905 &	503
Atropine, Valerianas, 1/60 gr....		213	" Botulinus ...		509
" with Ether ...		105	" Bouchard's = B. Bulgari-		
Atta ...		506	cus ...	58, 10	
Attar of Rose	876 &	166	" Bulgaricus ...	57 et seq.	10
Auld's Non-specific Protein			" Butter ...		601
Therapy ...		667	" Caucasicus ...	57 et seq. &	10
Aural Bougies ...		218	" Coli Communis ...	914 &	533
Auramine ...	322 &	270	" in Urine, 391; in		
" Emetine Periodid			Water ...	436-442	
1 gr. <i>q.d.</i> ...		537	" Differences between B.		
" in Anthrax ...		906	Coli & B. Typh. ...	436	
<i>Aurantii Cortex</i> , 842; Flor. ...		46	" Diphtheriæ ...	915 et seq. &	534
Auremetine, 1 gr. <i>q.d.</i> ...		537	" Diphtheroid ...		536
Auri Brom. 1/64 to 1/5 gr. ...		218	" Doderlein ...		610
" Chlor., 1/64 to 1/16 gr. ...		218	" Dysenteriæ ...	917 &	541, 544
" Cyanid, 1/60 to 1/12 gr. ...		270	" Enteritidis ...		439, 509
" et Potassii Cyanid.. 1/64			" Friedländer ...	908 &	567
to 1/3 gr. ...		219	" Fusiformis (Vincent's		
" et Sodii Chlor., 1/30 to			Angina) ...	926, 1097	
1/12 gr. ...		219	" Gartner's ...		509
" Trichlor., 1/64 to 1/16 gr. ...		218	" Gas Gangrene ...		546
Auricular Fibrillation ...	393,	721	" Glands ...		547
Aurin ...		189, 418	" Glycobacter ...		57
Aurinaria ...		218	" Gunther's ...		11
" Cocain. Hyd., 1/10 gr. ...		337	" Hoffman ...		536
" Hydrarg. Nit. ...		466	" Huppe's ...		11
" Scarlet ...		313	" Influenzæ ...	906, 921 &	550
Aurocyanase ...		221	" Klebs-Löffler		
Aurum ...		218		915 et seq. &	534
Australene ...		148	" Koch-Weeks... ..		536
Autoclaves ...		259, 261	" Lepræ ...		554
Autunite ...		323, 355	" Malignant Oedema ...	546,	559
Ava, Awa Root ...		865	" Mallei ...		547
Avantine ...		122	" Massol ...		10
<i>Avena Sativa</i> , 842; Avenyl,			" Mesentericus ...		560
613; Avertin, 246; Aviation			" Morax-Axenfeld ...		536
Spirit, 144; Azadirachta ...		842	" Oedematis Maligni ...	546,	559
Axungia ...		835	" Oppler-Boas ...		418
Ayahasco ...		845	" Paratyphosus ...	948 &	509, 606
Azafran, F.E. = Saffron.			" Perfringens ...		546
Azahar (Flores., F.E. = Aur-			" Pestis ...		562
antii Flores ...		842	" Pfeiffer's ...	921 &	550
Azobenzol and comps. ...		310	" Pneumo, Friedlander ...	908	
Azotite d'Amyle. ...		153	" Pneumosintes ...		923
Azur I. and II., Azur II.-Eosin.		575	" Proteus ...		568
" B.E." ...		939	" Pyocyaneus ...		265
" B.I.P.P." ...		234	" Putrificus ...		12
			" Rheumaticus ...		927

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE
Bacillus, Septus	908
" Shiga's ...	917 & 541	
" Sporogenes ...	12, 547	
" Subtilis ...	259	
" Suipestifer ...	509, 550	
" Sulphur ...	438	
" Tetani ...	931	
" Timothy Grass ...	601	
" Tuberculosis 934 & 391,	593	
" " Human & Bovine differences ...	593	
" " in Butter, 490; Fæces, 600; Milk, <i>see</i> Milk, Urine, etc. ...	391	
" Staining ...	598, 601	
" Typhosus and P-typhi 948 <i>et seq.</i> & 603		
" " in Urine ...	391	
" " in Water ...	438	
" Vaginæ ...	610	
" Variability of ...	533	
" Vincent's Fusiform 926, 1097		
" Welchii, 12, 546; Serum 10 Cc. used in Peritonitis and Toxæmia 1094		
" Whooping Cough 956 & 612		
" Wisp' ...	505	
" Xerosis. ...	536	
Bacteria, Acid-fast ...	598, 599, 601	
" Digestibility of ...	899	
" Mutability of ...	533	
" Pathogenicity of ...	897	
" Preservation of ...	620	
Bacterial Emulsions ...	901	
Bactericides. <i>See</i> 30 <i>et seq.</i> & 262		
Bacterins ...	895 <i>et seq.</i>	
Bacteriological Notes ...	503	
(<i>See also</i> Bacilli).		
Bacteriolysins ...	897	
Bacteriophages ...	899, 544	
Baculum Chrysarobini ...	295	
" Resorcini ...	752	
Badiane ...	843	
Bael Fruit ...	844	
Bain de Vichy ...	772	
Bain dit de Vichy ...	772	
Bakers' Dermatitis ...	1051, 116	
Baking Powders ...	114	
" " Alum in ...	115	
Balm ...	870	
Balmain's Paint ...	334	
Balmosa ...	73	
Balnea = about 25 gallons.		
" Alk. = Sodii Carb. 6 ozs. - 50 galls.		
" Amyli, $\frac{1}{2}$ lb. ...	299	
" Bituminis ...	299	
" Boracis, 2 ozs. ...	709	
" Furfuris (Bran.), 4 lbs. ...	770	
" Picis Carb. ...	770	
" Potassæ Sulphuratæ ...	782, & 799	
" Salinum ...	625	
" Sulphuris, 700; Alk. ...		
Balsam Aniseed ...		

NAME.	DOSE.	PAGE
Balsam Canadense	162
" Copaibæ	624
" Fioraventi	702
" Gurjunæ, $\frac{1}{2}$ to 2 dr.	843
" Lanolinatum	843
" Locatelli	702
" Peruv., 5 to 15 m.	843
" Tolut, 5 to 15 gr.	843
" Vitæ Hoffmanni, 1 to 4 dr.	811
Bamber Oil ...	129, 556	
Bandages ...	260, 270, 435	
Bandrowski's Base ...	33	
Banisterine ...	165	
Banting ou Insulin ...	640	
Baptisia (Baptisin, 1 to 5 gr.) ...	843	
Barberry ...	844, 57	
Barbitalum, 5 to 10 gr. ...	817	
" Soluble, 5 to 10 gr. ...	819	
Barbitonum, 5 to 10 gr. ...	817	
Bardana ...	866	
Barfoed's Test ...	376	
Barii Acetas ...	844	
" Carbonas ...	222	
" Chloridum, $\frac{1}{2}$ to 1 $\frac{1}{2}$ gr. ...	843	
" Hypophosph. $\frac{1}{2}$ to 1 gr. ...	691	
" Nitras ...	844	
" Oleas ...	604	
" Peroxidum ...	494	
" Sulphas ...	222	
" " Gelatineux ...	222	
" Sulphid., $\frac{1}{2}$ to 1 gr. ...	221	
" " Depilatory. ...	221	
" Thiosulph. ...	222	
Barium Platino Cy. Screens ...	292	
" Water ...	843	
Bariumised Wool ...	222	
Barker's Injn. ...	351	
Barley ...	506	
Barosma, var. ...	845	
Barr, Sir. J., on Lime Salts ...	255	
Basal Metabolic Rate ...	992	
Basham's Mixture, av. 4 dr. ...	416	
Basil ...	875	
Bassia, var. ...	844, 164	
Bassorin (Lasiosiphon) Paste ...	867	
Bath Water ...	443	
Baths, Artif. Sea Water ...	770	
" Nauheim and Salt ...	257, 779	
" Sod. Bisulph. ...	779	
Battiste ...	435	
Battley's Liq. Opii ...	629	
Baume Analgésique ...	73	
" de Fioraventi ...	702	
" de Vie = Dec. Aloes Co. ...	—	
" Tranquille ...	501	
Bay Berries ...	867	
Bay Rum. ...	118	
Bayer '205' ...	314, 534, 593	
Baylahuen ...	854	
Bazin's Ointment ...	476	
Bearberry Leaves ...	841	
" Bark (misnomer) ...	57	
Bebeeru Bark ...	844	
Beberin HCl. and Sulph. ...	844	

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Becker's Solution	46	Benzoyl-Hydrate, 5 to 15 gr....	...	66
Beck's Bismuth Paste	233	-Morphine	1399
Bee Tincture	841	-Naphthol, 4 to 10 gr.	572
Beech Tar	705	-Peroxide	66
Beecham's Pills	625	-Pseudo-Tropine	3433
Beechwood Creosote	383	-Salicin...	878
Beef Preps., 581; and Malt	...	582	-Sulphonic-Imide	754
Wine	582	-Tetrameth-di-amino-	...	3455
,, Peptone with Malt, 2 to 4	...	664	eth.-di-meth.-carbinol	...	3122
dr.	639	Benzyl Acetate	3122
,, Peptonised Jelly of	582	,, Aceto Salicyl	311, 4422
,, Tea Conc.	493	,, Alcohol	311, 4422
Beer	755	,, Benzoate, 2to6m.(diluted)	...	2166
Beet Sugar	438	,, Carbinol	3122
Beggiatoa	896	,, Chloride	3100
Behring on Diph. Antitoxin...	...	844	,, Cinnamate	3100
<i>Bela Fructus</i>	—	,, di-chloride	5677
Beleno, F.E.=Hyoscyamus	...	641	,, Morphine Tart.	3122
(leaves, seeds)	46	,, Succinate	3100
Belgian Glossary	48	Benzylidene Chloride	9455
Belladonna Leaves, 1 gr.	...	48	Beraneck's Tuberculin	1644
,, Fruit	224	Berberine Carb., HCl., Phosph.,	...	844, 1644
,, Indian	223 & 46	Sulph., 2 to 6 gr.	844, 1644
,, Plasters	46	<i>Berberis</i> var.	1322
,, Root, $\frac{1}{2}$ gr.	1444	Bergamot	5055
,, Assay, etc..	...	371	Berginisation	2738
Bence Jones Albumose	638	Beri Beri 593, 877, 1035 &	...	1037
Benedict's Tests (and Modifs.)	...	662	Berkfeld Filter	5883
Benger's Food	625	Berlece's Solution	8355
,, Liq. Pancreaticus	876	Berna Milk	2933
,, Pepticus	310	Bernsteinsäure (Ac. Succinic)	...	898, 950
Bengue's Balsam	323	Beryllium Tubes	349
Benné Oil	32	Besredka on Vaccines <i>per os</i>	...	344
Benzal Chloride	344	Beta-Borocaine, $\frac{1}{2}$ grain	...	344
Benzaldehyde, $\frac{1}{2}$ m.	309	,, - Borate, $\frac{2}{3}$ gr.	349
,, Green	393	Betaine HCl., 1 to 8 gr.	216
Benzaldehyde-HCN	394	Beta Vulgaris	5
Benzamine (HCl.) 1/10 to $\frac{1}{2}$ gr.	...	350	,, -Eucaine, HCl., 344; Lact.	...	344
<i>Benzaminæ Lactas</i> , $\frac{1}{2}$ to $\frac{1}{2}$ gr....	...	754	$\frac{1}{2}$ to $\frac{1}{2}$ gr.	344
Benzene, 5 to 10 m.	6, 2	Beta-Naphthol, 3 to 10 gr. 570 & 6,	...	275
Benzidine	410	,, Benzoas, 4 to 10 gr.	572
,, and Sod. Perbor. Tabs....	...	216	Salicyl	572
Benzine	310	<i>Betel</i>	841, 844
Benzocaine, 3 to 8 gr.	310	Betol, 3 to 8 gr.	572, 216
Benzoic Sulphimide	310	Bettendorf's Reagent	36
<i>Benzoin</i> , Siam, Sumatra	...	310	Betula Alb.	705
Benzoin Reaction in C.S. Fluid	...	310	Betula lenta, 72; Betulol	...	73
<i>Benzol</i> , 5 to 10 m.	313	Bhang	266
,, Capsules, 5, 10, 15 m.	...	144	Bial's Test	379
,, Chloride	869	Biddie	26
Benzol - azo - Benzol - azo - B-	...	309, 659	Bieber's Reagent	135
Naphthol	572	Biebrich Scarlet	313, 61
,, Mixture	697	Bikh	835
Benzo-Mastiche	703	Bilberry	872
Benzoline	413	Bile Beans	625
Benzonaphthol, 4 to 10 gr.	...	447	Bile Tests	365
,, Varnish	754	Bilharzia (and Therap. Ind.)	...	162, 471, 529
Benzo-Piperaz., 2 to 5 gr.	...	508	Biliary Antiseptics	451
Benzo-purpurin	350	Bilious remittent fever	613
Benzosol, 4 to 12 gr.	8 & 208, 331	Billroth's Cambric	435
Benzosulphinidum	331	Biloptin	682
Benzoyl-Chloride	331			
,, -Ethyl-dimethyl-amino	...	331			
propinol HCl.	331			
,, -Glycocol	331			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Bilsenkraut = Hyoscyamus ...		501	Bismuth Paraffin Emulsion, 1		
Bimital ...		193	oz. <i>mane</i> ...		657
Biniodide Lotion, Solubes and			" " Injection ...		233
other preps. 463 <i>et seq.</i>		83	" Paste (Beck's) ...		233
Soap .		465, 761	" Phenas, 10 to 30 gr.		237
' B.I.P.P.' ...		234	" Pot. et Sod. Tart. ...		239
Bi-quinyl ...		243	" " Sterules ...		242
Birch Tar, 705; Birch, Sweet.		65	" Potass Tartrates ...		239
Bird Lime (Japanese) ...		894	" Pyrogallas, 2 to 8 gr.		238
Birth Control ...		729	" <i>Salicylas</i> , 232, 49, 216		
Bisedia, 1 dr. ...		229	" Sod. et Pot Tart. 239, 49		
Bish ...		835	" " Sterules ...		242
Bisciniod, $\frac{1}{4}$ to 1 gr. ...		230	" Sod Tart <i>Neut.</i> ...		238
Biscuit Foods ...		587	" Sod Tart <i>Acid</i> 2 to 5		
Bishop's Method ...		629	gr. ...		239
Bismarck Brown ...		535	" <i>Subcarb.</i> , 5 to 20 gr.		227
Bismolan ...		625	" Subgallas, 8 gr. 236, 216		
Bismosal, $\frac{1}{2}$ to 1 dr. ...		229	" Subiodas ...		834
Bismostab ...		242	" <i>Subnitrates</i> , 5 to 20 gr.		
Bismuth Metal for injn. ...		242	233 & 49		
Bismuth in Syphilis ...		240	" Subsaliacyl, 5 to 20 gr.,		
Bismuth and Soamin ...		241	233; Basic. ...		232
" Comps. Organic ...		49	" Sulphocarb., 4 to 8 gr.		233
Bismuth Acetamino-oxyphenyl-			" Tannas, 10 to 30 gr.		237
arsenas ...		193	" Tartras Solub., 2 to 5		
" Alkali Tartrates ...		238	gr. ...		239
" Alloys ...		48	" Test Meals ...		228, 232
" Arsanilas (Shircore) .		241	" Tribromphenas, 5 to		
" Benzoas, 5 to 20 gr. 227, 216			20 gr. ...		20
" <i>b-naphtholas</i> ...		237	Bismuthyl ...		242
" Bronze ...		48	" Tartrates ...		238
" Carbolas ...		237	Bismutol Sterules ...		242
" <i>Carb.</i> , 5 to 20 gr. 227, 49			Bismutose, 15 to 30 gr..		237
" Cinch. Iodid., $\frac{1}{4}$ to 1 gr. 230			Bistovol ...		193
" Citras, 2 to 5 gr. 229, 216			Bisurated Magnesia, $\frac{1}{2}$ dr.		545
" Gauze... ..		229	Bisuroids ...		630
" Colloidal ...		365	Bites, Insect ...		1036
" et Ammon. Citr., 2 to			Bitter Apple, 2 to 8 gr.		380
5 gr. ...		229	Bitter Bush ...		849
" et Cerii Salicyl., 5 to			Bitter Sweet ...		887
20 gr. ...		233	Bitter-free Cascara, $\frac{1}{4}$ to $\frac{1}{2}$ dr. .		278
" Emetine Iodide ...		531	Bitumarine ...		300
" Gallas, 8 gr. ...		236	Bitumen... ..		300
" Hydroxyd, 5 to			Biuret Reaction 95, 363, 364, 532		
20 gr. 231, 243, 49			Blackberry, Norwegian		882
" Meals ...		228, 232	Black Draught, 1 to 2 ozs.		886
" Mucilago ...		232	" Haw ...		493, 894
" Nitras Cryst., 5 to 10			" Precipitate ...		458
gr. ...		231	" Wash ...		475
" Nucleinas, 20 to 40 gr. 281			Black-water Fever 737, 1037 & 508		
" Oleas, 5 to 10 gr. ...		604	Blair Bell's Calcimeter... ..		405
" Organic derivs. ...48-50			Bladder Wrack .		858
" Oxide hydrated ...		231	Blair's Gout Pill ...		625
" Oxidum, 5 to 20 gr.,			Blair's Tooth Pdr. ...		253
231, 243			Blanc de Baleine ...		849
" Oxybenzoas... ..		227	Blanc de Perle ...		231
" Oxybrom, 5 to 7 gr. 232			Blastomycosis 509 & Therap. Ind.		
" <i>Oxycarb.</i> , 5 to 20 gr. 227			<i>Blaud's Pill</i> ...		412, 79
" Oxychlor, 5 to 20 gr. 231			Bleaching Pdr. ...		45, 53
" Oxyiodid., 5 to 10 gr. 232			Blenosan ...		624
" Oxyiodogallas 236, 216			Blepharis Cap ...		844
" <i>Oxynitrates</i> , 5 to 20 gr. 233			Blighia Sapida .		844
" <i>Oxysaliacyl</i> , 5 to 20 gr. 232			Bliss' Cure ...		717
" 'Panama' ...		528, 537	Blistering Fly ...		267 <i>et seq.</i>
" Pancreatin, 1 to 2 dr. 230			<i>Blistering Liquid</i> ...		269

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Blood Agar	618	Books, to Disinfect	2722
„ Benzidene Test for	393	Boracite, 60 grs.	111
„ Bilirubin	611	Borage	506, 889
„ Calcium in	404	Borated Hydrogen Peroxide	4955
„ Carbon Monoxide in	501	<i>Borax</i> , 5 to 20 gr.	12, 38
„ Coagulability of... ..	254, 402	402	Borax Carmine	4011
„ Colour Index	396	Bordeaux Bx.	314
„ Corpuscle Tests : Estn....	...	395	Bordet-Gengou Reaction
„ in Fæces...	411	„ Gono. 550 ; Syph., 579 ;
„ Guaiacum Test	392	„ Tuberc.	6022
„ Hæmachromogen Test...	393	Bordet's Vaccine	9563
„ Hæmoglobin Estn.	394	Boric Acid and Starch Powder
„ Hyd. Ion Concentn.	403	and with Zinc	829
„ Kastle-Meyer Test	394	Boric Cream	11
„ Leucocyte Count	396	„ Gauze, Lint & Wool	9
„ Lime Salts in	255	„ Petroleum Jelly	11
„ Phenols	405	Borneol Salicyl	733
„ Platelets...	401	Borneol-isovalerianate	8263
„ Potash content...	405	Bornyl Acetate	1363
„ Precipitin Test	392	Borocain, $\frac{1}{2}$ to $1\frac{1}{2}$ grains	133, 349
„ Pressure 154, 579, 717, 1038,	...	402	Boron	3
„ ‘ Purifiers ’	884	Borovertin, 15 to 60 gr.	452
„ Reaction of	402	Borrel's Blue	558
„ Root	884	Borrelia recurrentis	568
„ Serum (Löffler's)	535, 619	619	Bosch Yaws	552
„ Staining	398	Botany Bay Kino, 5 to 20 gr....	...	856
„ Sugar Estn.,	405-406	406	Botulism and Antitoxin	1039, 509	509
„ <i>See also</i> Insulin.	Bouchard's Remedy	42
„ Tests	393	BOUGIES , 244, 270 ; Aural	218
„ Thymolphthalein Test...	394	„ Nasal, 244 ; ‘ X ’ Ray	294
„ Transfusion	995	„ URETHRAL GELATIN ,
„ Urea Estn.	384	2 $\frac{1}{2}$ and 4 in. (dip in
„ in Urine	392	warm water)	244
„ Viscosity of	402	„ Argent. Proteinate,
Blosser's Remedy	717	$\frac{1}{2}$ grain	177
Blue Alkali, Aniline	2	„ Bellad, Alc. Ext., $1\frac{1}{2}$ gr.	—
„ Gum Tree (Eucalypt.)	613	„ Bellad. Ext. $1\frac{1}{2}$ gr. etc.
Blueberry	872	Ext. Opil., 1 gr.	—
Blue Methylene, 1 to 4 gr.	325	„ Cocaine, $\frac{1}{2}$ gr.	334
Blue, Nicholson's, 2 ; Night,	„ Cotarnine HCl., $\frac{1}{2}$ gr.	574
325 ; Opal, 2 ; Patent	„ Ext. Krameria, 1 gr.	—
A, 325 ; Spirit, 2 ;	„ Leistikow's	177
Water Soluble	2	„ Neisser's	177
„ Uncion, 457 ; Pill	456	„ Opium, 1 and 2 gr.	—
Boas' Test	415	„ Silver Nitrate, $\frac{1}{2}$ gr.	—
Body Vermin. <i>see</i> N.C.I., Vermi-	„ Stypticin, $\frac{1}{2}$ gr. to $\frac{3}{4}$ gr.	—
jelli, Lefroy's Emulsion, also	„ Thalline, 1 gr. and 2 gr.	—
Parasites	1081	„ Zinc Acet., Chlor. and
Boeck's Egg Med., 619 ; Lotion	Sulph. $\frac{1}{2}$, $\frac{1}{2}$ and 1 gr. etc.	—
and Liniment	706	„ Zinc Sulphocarbolate, $\frac{1}{2}$ gr.	—
Bogbean...	870	„ URETHRAL WITH CACAO
Bog Moss	785	BUTTER (dip in Catheter
Bohadschia Aphrodisiaca	854	Oil)	244
Boldoa Fragans	844	„ Bellad., Ext. Rad., $\frac{1}{2}$ gr.
Boletus Laricis, 10-30 gr.	836	„ Bismuth Oxychlor., 5, 10 gr.
Bolton, John A. on Washing...	762	and c. Lead Acet, 1 gr.
Bolus Alba	142	„ Cocaina, $\frac{1}{2}$ gr.	334
Bonain's ‘ Mixture ’	334	„ Copper Oleate, 5 gr.	602
Bonduc Nut	844	„ Cotarnine HCl., $\frac{1}{2}$ gr....	...	574
Bone Marrow Extract, Red	958	„ Eucalyptus Oil, 10 m.	—
Bon Voyage $\frac{1}{2}$ oz., 41 ; Tabs....	...	42	„ Eucalyptus Oil, 10 m....	...	508
Bonney & Browning's Violet	„ Iodoform, 5 grs.	—
and Green	324	„ Iodoform, 3 and 5 gr.	—
			„ Lead Acetate, $\frac{1}{2}$ gr., $\frac{1}{4}$ gr.	48
			„ Mercuriome	48

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME	DOSE.	PAGE
BOUGIES , Neisser's	177	Brom-iso-valerianyl-urea	...	821, 218
„ Opium, 1 and 2 gr.	—	Bromo-cresol purple	187, 608
„ Orthoform, 5%...	346	„ phenol blue	187
„ Potass. Permang., $\frac{1}{2}$ gr.	555	„ Thymol blue	187
„ Proflavine, $\frac{1}{2}$ gr.	306	Bromol, $\frac{1}{2}$ to 2 gr.	20
„ Silver Nitrate, $\frac{1}{2}$ gr.	175	Bromo-protein, 10 gr.	246
„ Stypticin, $\frac{1}{2}$ gr.	574	Bromo-Ray, 4 to 7 Gm.	686
„ Tannic Acid, 1 gr., and	...	—	Bromphenobis, 5 to 20 gr.	20
„ with Opium, 1 gr.	—	„ Gauze	20
„ Zinc Chlor. and Sulph.,	...	—	Brompton Blacks	860
„ $\frac{1}{2}$ to 1 gr.	—	Brompton Cough Specific	626
„ Zinc Permang. $\frac{1}{2}$ gr.	556	Bromsulphalein...	147
Bouveau Huile de,	705	Bromum	244, 50, 270	
Bovril	581	Bromural, 5 to 10 gr.	821 & 218	
Bow's Liniment	625	„ Tablets, 5 gr.	821	
Brachylæna Elliptica in	...	—	Bronamalt, 1 to 2 dr.	550	
diabetes.—J. M. Watt, P.J.,	...	—	Bronchial Asthma, Peptone in	667	
June 30/28, 602.	...	—	Bronchial Glands	961	
Brain Extract	959	Bronchiectasis, Iodinol in ...	87	
Brand's Meat Juice	582	„ Lipiodol in	521, 88	
„ Nutrient Pdr.	583	Bronchitis, Vaccines in	907	
Brandish's Solution	709	(See also Therap. Ind.).	...	
Brandy	118 & 26		Bronchoscopic Insufflation ...	228	
Brass Oil	391		Brooke's Ointment	602	
Brass Paste	390		Broom	784	
„ „ Picric	391		Broth, Nutrient	617	
Brassica var.	763		Brownian Movement	362	
Braxy	547		Browning on Acriflavine 301 <i>et seq.</i>		
Bread and Flour	107		„ Brill. Green	324	
„ in London Tea Shops... ..	121		Brown's Bronch. Troches	626	
„ making	118		Brucea Sumatrana	844	
„ North Country	121		Brucine and Salts, 1-12 to $\frac{1}{2}$ gr.	844	
„ Potato Starch in	117		Brunol	73	
„ Report Dept. Com. on	...	—	Brunton's Snake Lancets	554	
„ Chemicals in... ..	120		Bryant's Sherry	519	
„ Standardisation... ..	107		Bryony	845	
„ Starchless	591		Bryone (Jalap)	864	
„ Vitamin B in	111		Bryonia (<i>var.</i>)	845	
„ Wholemeal <i>v.</i> White	107		Buba	552	
„ Yeast used for making... ..	111		Buchu	845	
Breast Feeding	588		Buckbean	870	
Bredig's Process	366		Buckthorn	858	
Brilliant-Green	324 & 270, 607		Buffer Solutions and Salts ...	191	
„ Ointments	325		Buginaria.—Nasal Bougies,	...	
British Spas	459		Elastic Gelatin, 3 $\frac{3}{16}$ in. long	244	
Broadbent's Mixture $\frac{1}{2}$ oz. ...	739		Buginarium Ac. Borici, 5 gr.;	...	
Brom-Albumen, 10 grs.	246		Ac. Carbol., $\frac{1}{2}$ gr.	
Bromal Hydrate, 2 to 5 gr. ...	245, 216		„ Cocainæ HCl., $\frac{1}{2}$ gr.	
Bromalin, Br.-ethylformine, 5	...	—	„ Cupri Sulph., 1-10 gr.	
to 30 gr.	245, 216		„ and $\frac{1}{2}$ gr.	244	
Bromeikon... ..	686		„ Iodof., $\frac{1}{2}$ gr. and $\frac{1}{2}$ gr.	
Brometone, 5 gr.	246, 216		„ Zinci Sulph., 1-10 gr.	
Bromides, 244; Estim.	152		„ {Aluminis, 1-10 gr.	
Bromidia, $\frac{1}{2}$ to 1 dr.	283, 625		„ {Zinci Sulph., 1-10 gr. ...}	...	
Bromine Sterules	244 & 383		Bugloss	855	
„ in Org. Comps., libera-	...	—	Bugs to kill	1081	
„ tion of	85 & 50		Bulgarian Bacillus	57 <i>et seq.</i> , 10	
„ Paraffin	519		Bungpagga	511	
Brominol (10%), $\frac{1}{2}$ oz.=20 gr.	...	—	Bunter's Nervine	626	
„ Pot. Brom.	245		Burdock	866	
„ (33%), 10-60 gr.	245		Burgess' Oint. and Pills ...	626	
„ Mixture, $\frac{1}{2}$ oz.	245		Burgi's Theory	569	
Bromocarpin, 1 dr.-1oz. acc. to age	696		Burgundy	26	
Bromodiethyl-Acetyl-Urea ...	820		Burgundy Pitch	704	
Bromoform, $\frac{1}{2}$ to 2 m.	246, 216		Burn, J. H., on Pituitary	968, 969	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Burn, on Ergot	403	Caffeinæ Valer., $\frac{1}{2}$ to 3 gr.	252
Burns, Paraffin Treatment	654	Caffeine-Chloral, 3 to 8 gr. hyp.	252
See also 1041			Cajuput, 845; Cajuputol	614
Burnet, Great = Sanguisorba off. (<i>Rosaceæ</i>)			Calabar Bean, 1 to 4 gr.	692
Burney Yeo's Catarrh Mist., 149, Chlorine and Quinine Mixture, 1 oz.	737	Calabaza F.E. = Cucurbita	829
Burow's Solution	140	Calamina Præp.	829
Burri's Ink	577	Cal Apagado, = Calc. Hydras.	258
Burt's Fluid	300	Calcidin	777
Busserole	841	Calcii Aceto Salicyl, 5 to 15 gr.	188
Butcher's Broom Tar	705	„ Bisulphid	511
<i>Buteæ Gummi</i> , 866; <i>Semina</i>	845	„ Bromid., 10-20 gr.	186
Butol Emulsion	598	„ Cacodylas, $\frac{1}{2}$ to 2 gr.	522
Butter Analysis	489	„ Carbide	253
„ B. tuberculosis in	490	„ Carb. Præcip., 15 to 60 gr.	253, 533
„ of Antimony	33	„ Chloridum, 5-15 gr.	254
„ Nut	864	„ as hæmostatic	522
„ of Orris	864	„ Cyanamidum	15 to 45 gr. . .
Buttercloth	435	„ Dibromobehenate	523, 218
Buttermilk	60, 10	„ Fluoridum, $\frac{1}{4}$ to $\frac{1}{2}$ gr.	833
<i>Butyl-Choral Hyd.</i> , 5 to 20 gr.	247, 218	„ Formas, 3 to 5 gr.	35
Butyl-Ethyl-Malon-Urea	821	„ Glyceroph., 3 to 10 gr.	36, 7, 218
Butyl Salicylate	73	„ „ Solubilis	37
Butyn	354, 69	„ Guaiacol-Sulphonat.	448
Butyric Ether	840	„ Hippuras, 5 to 20 gr.	8
Buxine	844	„ Hydras	260
Bynin (et Amara), 2 to 4 dr.	549, 626	„ Hypochlor. (Chlorinat.)	45
Bynol	626	„ Hypoph., 3 to 10 gr.	690
Byno-Lecithin, $\frac{1}{4}$ oz.	540	„ Iodas and Preps., 3 to 4 gr.	834
Bynoplasma, $\frac{1}{4}$ oz.	973	„ Iodidum (in dilute solution), 2-4 gr.	258
Bynotone	959	„ Iodobehenas	522
Cacao and Cacao Butter	804	„ Iodo-Ricinoleas, 3 gr.	622
C. B. Q. Tabs. and Lin.	626	„ Lactas, 10 to 30 gr.	55, 254 et seq. 213
C. E.	288	„ Lactoph., 3 to 10 gr.	56
Caapi	845	„ Margosas	843
Cabalonga de Tabasco	600	„ Monosaccharate	260
Cachets	698	„ Naphthol-sulphonas, 10 to 30 gr.	362
Cachets, Oxyquinotheine	252	„ Nitras	53
Cacodyle, 185; "New"	188	„ Oleas	604
Cacodyl Oxide	185	„ „ Colloidal	370
Cacodyliacol, $\frac{1}{2}$ to 2 gr.	186	„ Permanganas	555 & 276
Cactus, 849; Cactina Pellets	849	„ Peroxid., 3 to 10 gr.	259
Cæsalpinia Bonducella	844	„ Phosph., 5 to 15 gr.	259
Cadmium, 164; Sulphate	37	„ „ Acidus, 5 to 20 gr.	259
„ Tungstate	293	„ „ Di-Acid, 5 to 20 gr.	259
Cadum	626	„ „ Di-basic, 10 to 30 gr.	259
<i>Caffeina</i> , 1 to 5 gr. . .	248 & 51, 218		„ „ Monoacid, 10 to 30 gr.	259
Caffeinæ Citras, 2 to 10 gr. . .	249, 218		„ „ Monobasic, 5 to 20 gr.	259
„ „ Eff., 1-2 dr.	250	„ Saccharas, 8-30 gr.	260, 218
„ Di-iodo-hyd.	251	„ Sulphas, 20-30 gr.	260
„ HBr., $\frac{1}{2}$ to 5 gr.	250	„ Sulphid., $\frac{1}{4}$ to 1 gr.	260
„ HCl., $\frac{1}{2}$ to 5 gr.	250	„ Sulphis	18
„ Hydriodid., $\frac{1}{2}$ to 5 gr.	250	„ Sulphurat. Sol.	261
„ Salicyl., 1 to 4 gr.	250	„ Superoxidum	259
„ Sodio-Benz., max. 45 gr. <i>p.d.</i>	250	„ Tungstas	295
„ Sodi Iodid., 2 to 10 gr. . .	252		Calcinol, 3 to 4 gr.	834
„ Sodio-Sal., 1 to 5 gr. . .	250, 52		Calcium 52, and the Blood . . .	254, 404	
„ Tri-Iodid., 2-4 gr. . .	218		„ Carbide	52
	251		„ Colloidal	370
			„ Deficiency and Parathyroid	994

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Calcium Diuretin, 7 to 15 gr....		806	Cancer Brit. Empire Campaign		517
„ Estimn. in Blood and			„ of Buccal Cavity		514
„ Urine ...		404	„ Causation ...		519, 523
„ Hydride ...		141	„ Cell ...		518, 520
Calculi ...		367	„ of Cervix Uteri (and <i>see</i>		
Calendula ...		845	„ Radium and X-Rays)		514, 517, 518
Calf Lymph, Glycerinated, etc.		952	„ Chemotherapy in ...		515
Californian Syrup of Figs ...		626	„ Coley's Fluid in ...		531
Caliche ...		510, 85	„ Constitutional Disease .		522
Calmette-Guérin on Vaccina-			„ Death Rate ...		529
tion of Newborn ...		944	„ Diagnosis, 515, 521;		
Calmette's Ophthalmic Reaction		947	„ Oleic Acid Method... 521		
Calomet, $\frac{1}{2}$ to 5 gr. ...		473, 82	„ Diet in ...		512, 525
„ Cream ...		455, 475	„ and Diphtheroid B. ...		524
„ „ Lambkin, 10 m. .		475	„ Distribution of... 523, 524		
„ Duret's .		473, 82	„ Etiology of ...		514
„ Ointment ...		475	„ Fat Examination ...		521
Calorex Glass ...		778	„ Filter-passing Virus ...		526
Calorie Values of Food ...		97	„ Fluorescein in ...		531
Caloric Fluid ...		337	„ and Glycogen ...		524
„ Wool ...		273	„ „ Glycosuria ...		522
Calot's Creosoted Oils ...		659	„ Goat Serum in... 1042, 511		
Calotropis. <i>Syn.</i> Mudar I.C.			„ Gye's work on... 526		
Add. <i>See</i> Edn. XV., p. 852.			„ Imp. Res. Fund's Rep. 512		
Calox ...		259	„ Increase ...		520
Calumbæ Radix... 845			„ Internat. Conf. '28 ...		513
Calvert's Carbolic Acid ...		264	„ „ Cong. '13 ...		513
Calvert's Sugar Estn. ...		407	„ Iodophil Reaction ...		521
Calx Chlorinata ...		45, 53	„ Irritation 519, 520, 527		
„ Sulphurata, $\frac{1}{2}$ -1 gr. ...		260	„ Lead 372, 374, 511, 515, 530		
Cambogia, $\frac{1}{2}$ to 2 gr. ...		845	„ League Enquiry ...		518
Cambridge on Diabetes ...		1052	„ Lipase Theory... 521		
Cambridge's Reaction ...		380	„ Lymph-stasis precursor.—		
„ Modified Benedict Test 371			„ Handley, B.M.J. ii./29, 607.		
Camphine ...		699	„ Manchester Campaign... 517		
Camphoid ...		361	„ and Meat ...		525
Campho-Phenique ...		205	„ „ Metabolism ...		522
Camphor (and artif.), 2 to 5 gr. 262, 54			„ Min. Health's Repts. on 518		
Camphor Ball ...		263	„ Mule-spinner's... 517, 529		
„ Essential Oil of ...		262	„ Natural duration of ...		530
„ Linim. .		262	„ Occupational ...		515
„ Monobrom., 2 to 10 gr. 265			„ Paraffin and ...		527, 528
„ Salicyl., 1 to 5 gr. ...		265	„ and Protists ...		523
„ Synthetic ... 262 & 54			„ Radiology, 515 (and <i>see</i>		
Camphorated Carbolic Acid ...		15	„ Radium, 340, and 304)		
„ Chalk ...		263	„ X-rays in—Johnson, B.M.J.		
„ Chloroform ...		289	„ ii./29, 618.		
„ Wool ...		264	„ of Rectum ...		514, 518
Camphre de Persil ...		169	„ Rous Tumours... 527		
Canada Balsam, Xylol, etc. 162			„ Serum Diagnosis of ...		523
Canadian Hemp Root ...		170	„ Shaw Mackenzie on 521, 522		
Cancer ...		511	„ Sodium Oleate in 761, 521,		
„ Acid production in ...		531	„ 522, 530		
„ Antiscrum ...		530	„ of Stomach, 516, 521,		
„ Arsenic ...		527	„ 523; Chlorides in, 521, 523		
„ Begg and Cramer on chem-			„ Survivorship Table ...		530
icals.—L. ii./29, 697.			„ Tar and... 527, 528		
„ Betel-chewing ...		529	„ Theories on ... 523 <i>et seq.</i>		
„ Biochemical concep'n. of 512			„ Transmissibility ...		512
„ and Blood Alkalinity ...		531	„ Treatment ...		530
„ „ reaction of... 519			„ and Vitamins ...		524
„ Blumenthal on... 526			„ Young-Glover organism 525		
„ Botelho Reaction in ...		523	(<i>See also Therapeutic Index</i> , 1042)		
„ Breast ...		514, 517	Candle Nut Oil ...		866

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Canella Alba	138, 845	CAPS., Chlorodyne, 5 m.	290
Cane Sugar	755, 157	" Chloroform 5 m. & 10,	...	289
Cannabin Tannate	2 to 10 grs.	267	" 20, 30 & 60 m. Sterules	...	290
Cannabinol	266	" Chloromorph. Sol., 5 m.	...	263
<i>Cannabis Indica</i>	266 & 54	" Cinnamic Aldehyde, 1 m.	...	298
<i>Cannabis Sativa</i>	266, 845	" Cinnamon Ol. 2½ m. c.	...	312
Canned food poisoning	510	" Quin. 1 gr.	617
Cantharis, 1-16 to ½ gr.	...	267, 55	" Cinnoxyl	617
<i>Cantharidinum</i>	268, 218	" Cod. L. Oil, ½, 1 dr.	617
Canton's Phosphorus	260	" { Cod. L. Oil, 19 m., }	...	617
Caoutchouc and Liquor	...	270 & 56	" { Creosote, 1 m., }	...	617
Cape Geranium	871	" and with Blaud P.	356
Cape Gooseberry	844	" Codein c. Ext. Cannabis	...	356
Capps's Method	187	" Codeinæ et Valerianæ	...	359
Caprokol, 2 to 10 gr.	753	" Comp.	624
" Capsules, 3 to 4 thrice	...	753	" Colchicine Salicyl. = 1/250	...	624
daily	753	" gr.	624
Caprylic Alcohol	385	" Copaiba, 5, 10, 15 m.	624
Capsicin, 1-20 to 1-10 gr.	...	271, 218	" { Copaiba, 5, 10 m. }	...	624
<i>Capsicum</i> , ½ to ¼ gr.	271	" { Cubeb Ol., 5, 10 m. }	...	624
Capsicum Gamgee Tissue	...	273	" Copaiba, 5 c. Santal, 5m.	...	385
" Wool	273	" Creocarb	386
Capsogen	273	" Creosotal, 5, 10 m.	387
CAPS., Gelatin (Gl = Glass)	...	698	" Creosote, 3, 5 m.	853
" Agrimony Ext.	837	" Creosote Valer., 8 m.	624
" Allyl Sulphid., ½, 1, 2 m.	...	837	" Cubeb Oil, 10 m.	32
" Ammonia (Gl.) 3 m.	148	" Cubeb, 5, c. Santal Oil,	...	54
" Ammon. Quin. = 1 dr.	...	738	" 5 m.	854
" Tinct.	738	" Cyllin, 1 and 3 m.	839
" Amyl Nitrite (Gl.), 1, 2,	...	153	" Cyperi Ext. Liq., 5 m....	...	854
3, 4, 5, 6, and 10 m.	...	73	" Damiana Ext., (30 m.	...	420
" Amyl Salicyl, 3 gr.	839	" Liq.)	169
" Amylene-Chloral, 8 m...	...	839	" Dormiol, 8 m.	405
" Amylene Hydrate, 10 m.	...	169	" Easton Syrup = ½ & 1 dr.	...	856
" Apiol, 3, 5, and 10 m....	...	169	" et aa. c. Arsen., 1/50 gr.	...	836
" 5 m.. Ergotin, 2	...	169	" Ergot and Apiol	111
" grs.	190	" Ergotin, 3 and 5 gr.	113
" Arsamin, 1 and 2 gr.	190	" Erigeron Oil, 5 m.	422
" 1 gr. c. Blaud 5 gr.	190	" Ethylene Bromide, 1 m.	...	374
" c. Quinin., 3 grs.	310	" Ethyl Chlor. (Gl. Spray	...	411
" Benzol, 5, 10 and 15 m.	...	312	" form), 3, 5, 7, & 50 Cc.,	...	412
" Benzyl Benz., 3, 5 m.	312	" also Tubes (local)	37
" Benzyl Succ. 5 gr.	312	" Ethyl Iodid. Co. (Gl.)...	...	698
" c. Papav. ½ gr.	412	" Ext. Filicis Liq., 15 m.	...	510
" Blaud Pill, 5 gr. (and	...	624	" Fehling's Sol. (Gl.)	...	698
comps.)	246	" 1 Cc.	40
" Blenosan	245	" Fel Bovinum, 5 gr.	623
" Brometone, 5 gr.	246	" Ferri Carb. Sacch., 5 gr.	...	445
" Brominol, 33%, 2 Gm.	622	" Ferri Glycero-ph, Co.	...	446
" Bromoform, ½ m.	555	" 1 t.d.	446
" Calc. Iodoricinoleate, 3	...	18	" Formalised Gelatin	446
grs.	277	" Formidin, 5 gr.	607
" Calc. Permang., ½ gr.	277	" Glutoid	582
" Carbol. Acid, 1 and 2 gr.	...	277	" Glyceroph. = ½ dr. & 1 dr.	...	40
" Cascara (mild)	277	" of Syrup	445
" Cascara (strong)	277	" Gonol	446
" (mild) c. Euony-	...	277	" Guaiacum Resin, 5 gr....	...	446
min, 1 gr.	620, 621	" Guaiacol, 2, 5 m.	446
" Castor Oil, ½, 1 dr. (and	...	170	" 1 gr., c. Iodoform,	...	446
Co.)	607	" 1 gr.	446
" Celery Oil, 3½ and 5 m.	...	418	" Guaiacol, ½ gr. c. Cod L.	...	607
" Chaulmoogra Oil, 5 to	...	248	" Oil, 5 m.	582
20 gr....	...	418	" Gynocardia (Chaulmoo-	...	582
" Chemical Food, 1 dr....	...	418	" gra), 5 to 20 gr.	582
" Chloretone, 5 gr.	418	" Hæmoglobin, 5 gr.	582

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
CAPS., Hydrastis=30 m. Ext.			CAPS., Sulphonal, 5, 10 gr. ...		795
Liq. ...		492	Syr. Easton, $\frac{1}{2}$ & 1 dr.		
Hypnone, $\frac{1}{4}$ min. ...		832	(et. c. Arsen) ...		420
Ichthosulphol, Amm.,			Syr. Fe Iodid. ...		417
or Lith., 4 gr., also aa.,			Syr. Fe. Ph. Co., 1 dr....		418
2 gr. ...		504	Terebene, 5 and 10 m....		803
Iodicin, 3 gr. ...		622	Terpinol, $1\frac{1}{2}$ m. ...		804
Iodinol 25%, 2 Gm. ...		519	Turpentine, 5, 10 m....		699
Iron Carb. Sacch., 5 gr. ...		412	Valerianatum Co., 1 t.d.		741
Iodide=10 & 30 m.			Capsuloids ...		626
Syr. ...		417	Capsungs' Hydrarg. Oleat Ung.		602
Izal 2 m. (& with Cod			Protargol Ointment ...		177
Liver Oil, 5 m.) ...		33	Ung. Prophylaxis ...		458
Kerol ...		33	Captol ...		283
Lecithin, $1\frac{1}{2}$ gr. ...		540	Caracol, F.E.=Helix Aspera et var.		
Male Fern Ext., 15 m. .		422	Caraway... ..		847
Menthol Paraffin ...		557	Carbamide, 10 to 60 gr. or more		815
Methyl Aspriodine, 5 &			Carbasus. <i>See</i> Gauzes		
10 gr....		87	Carbo Animals and Ligni		846, 164
Meth. Blue, 2 gr. ...		325	Carbohydrates ...		592, 94, 96
Myrtol, 2 and 5 m. ...		872	Carbol-Fuchsin Solution ...		598
Nisbet's Specific, 20 m. ...		623	Gentian Violet ...		615
Nitrite of Amyl			Methylene Blue ...		598
(Sterules) ...		153	Methyl Violet ...		615
Nitroglycerin, 1-100 and			Thionin ...		615
1-50 gr. ...		577	Carbolic Acid ...		13
Ol. Allii, $\frac{1}{2}$, 1, 2 m. ...		837	" Lotion ...		15
" Apii Graveolens,			Coefficient ...		262
$3\frac{1}{2}$ and 5 m. ...		170	Gauze; Oil ...		16
" Cedri Atlant, 8 m. ...		849	Carbolised Camphor, 15; Gauze		
" Chaulmoogra, 5-20 gr. ...		607	and Bandages, 16; Glycerin,		
" Elliott, $\frac{1}{4}$ m. (three			273; Iodine Sol., 17; Resin,		
to 5) ...		875	18; Smelling Salts, 18; Wool		16
" Gaultheria, 10 m. ...		72	Carbon Bisulphidum, 846, 270,		
" Turpentine, 5, 10 m. ...		699	557; Dichloride, 293; Dioxide,		
Oleic Acid, $7\frac{1}{2}$ m. ...		601	22; Monoxide ...		874, 501
Olive Oil, $\frac{1}{2}$, 1 dr. ...		619	Carbon, Number of Soaps ...		159
Ox Bile, 5 gr. ...		411	Carbon Tetrachlor., 10 to 45 m.		
Ovoma mmoid ...		964	in several capsules ...		274, 56
Papaveris ...		625	Carbonate Titrations ...		192
Paraffagar ...		658	Carbonised Cotton ...		439
Paraffin (for Catheters) ...		658	Carbon Tetrachlor, Iodised ...		276
Paraldehyde, 20, 30, 40m. ...		126	Carbonic Anhydride ...		22
Phenalgin ...		3	Carbonic Snow ...		22
Phosphorated Oil, 5 m. ...		688	Carbonite ...		575
Phosphorated Cod Liver			Carbonyl Chloride ...		816
Oil, $\frac{1}{2}$ dr. ...		689	Carborundum ...		295
Potass Iodide, 5 gr. ...		716	Carburetted Gas ...		501
Potass Permang., 1 gr... ..		552	Carbromalum, 5 to 10 gr. ...		820
Quin. Salicyl., 5 gr. ...		735	Carcinoma, 511, and <i>see</i> Therap.		
Sahl's ...		698	Index; Radium in, 340; X-		
Salol, 5 and 10 gr. ...		81	Rays ...		304
Santal and Kava ...		623	Cardamomi Semina ...		846
Santalol, 5 m. ...		622	Cardiac, Intra Injns. .		980
" 4 m. c. Methyl			Cargile Membrane ...		958
Salicyl., 1 m. ...		623	Carica Papaya ...		651
Santal Oil, 5 and 10 m.			Caresbad Salt, True and Artif.		780
c. Methylene Blue,			Carmalum ...		847
$\frac{1}{2}$, 1 and 2 gr. ...		623	Carmeliter Geist ...		870
Santal Oil, 5 to 20 m. ...		623	Carmine .		846
Savaresse, 10 m. ...		623	Carnauba Wax ...		248
Sod. Chaulmoograte A.,			Carnotite ...		323, 355
1, 2 and 3 gr. ...		607	Carnrick's Peptonoids		664 & 626
Sodium Oleate, 5 grs. ...		761	Carrageen ...		851
" " Co., <i>m. et n.</i>		761	Carrel-Dakin Treatment		50, 325

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Carron Oil	260	Cavendish Moss, 786; Water...	...	781
Carter's Little Liver Pills	626	C.E., 288; Cedar Wood Oil, 848;
<i>Carui Fructus</i>	847	Cedrene	848
Carum Copticum	809	Cedrol	848
Carvacrol	876	Cedrus Atlant	849, 1644
Carvonum	840	Celandine	850, 881
<i>Caryophyllum</i>	847	Celanese	440
Casca Bark	409	Celerina	253
Cascagar, 1 teaspoon to 2 table-	Celery	169
spoons	277	Cellafine	435
<i>Cascara</i> , 3 to 15 gr.	276 & 56	Cellon	59
,, Bitter-free, $\frac{1}{2}$ to $\frac{1}{2}$ dr....	...	278	Cellophane	435
,, Caps., 277; Pastils...278	...	278	Cellulase...	76
,, Jelly, 1 to 4 dr.	277	Celluloid, 361; Splints & plates	...	361
,, Cultivation	57	Cellulose Acetate Silk	440
,, Substitutes	57	,, Solvents	441
,, Wood	56	,, Films	435
Cascarets	626	,, Formate	442
<i>Cascarilla</i> , Cascarillin	848	,, Nitrate	440
Casein	589, 619	,, Solvents	441
,, Estimation	466	Wadding and Tissue	435
Caseinogen	589	Celmo	626
Cashew Nut	839	Cement, Portland	144
Casse en Batues	848	Cephaeline (and HCl.), Emetic
<i>Cassia Acutifolia</i> , <i>Angustifolia</i>	...	886	1/12 to 1/6 gr.	539
,, <i>Fistula and Pulp</i>	848	Cephaelis Ipecac.	524
,, <i>Fructus</i>	848	<i>Cera Alba</i> , <i>Flava</i>	849
Castela <i>Nicholsoni</i>	849	,, <i>Aseptica</i>	849
Castellani's Antimon. Tart.	Cerasin Red	313
Injn., $\frac{1}{2}$ to 1 Cc.	161	Cerato Laudanizado, F.E.=Sy-
Castellani's Ointment	752	denham's Laudanum, 1 to 9,
Castellani's Tetra and Penta	Ceratum, U.S., 654; Galeni,
and Hexa Vaccines...	949	876; Petrolei, 654; Resinæ...	...	881
Castile Soap	153	Cerebos Salt	770
Castoreum	848	Cerebral Extract	959
<i>Castor Oil</i> , 1 to 8 dr.	620	Cerebro-Spinal Fever	909, 532	...
Castor Oil Powders	621	,, "Carriers"	910
,, Solutions of Alkaloids	...	621	Cerebro-Spinal Fluid	408
Casts	368	Cereoli <i>vide</i> Bougies
Casumen	590	Ceresin	653
Catalase...	76	Cereus, Night-blooming.	849
Cataplasma Kaolini	431	Cerevisiæ Ferment, $\frac{1}{2}$ -1 oz.	279
Cataplasma Salicyl Co.	431	Cerii Oxalas, 3 gr.	849
Catarrh 1044, Vaccines for	907, 908	...	,, Oxidum	57
Catechol...	6	,, Sulphocarb., 1-5 gr.	849
<i>Catechu Pallidum</i> , 5-15 gr.	848	Cerium	57
,, <i>Nigrum</i> , 5-15 gr.	848	Ceruleinum	62
Catgut	541	Cerussa	707
,, Ligatures	541	<i>Cetaceum</i>	849
,, Absorbable	542	Cetraria	849
Catha	847	Cetyl Alcohol (and Palmitate)	...	849
,, Cocoa Milk	848	Cevadilla Seeds, Cevadine	893
,, Milk and Glyceroph.	848	Ceyssatite, 144; Chalk's Bottles	...	214
,, Phenolphthalein Eff.	848	Chagas' disease...	538
Catheters	270	Chalk, Camphorated	263
Catheter Oil, 16; Salol Oil	82	<i>Chalk Mixture</i> , $\frac{1}{2}$ to 1 oz.	253
Catheter Lubricant, 16, 460,	Chamberland Filters	278
655; (Adrenalin), 982; Surgi-	Chamomile Flowers	506, 840	...
cal Lubricant	16	Champagne	26
Cathode	279	Chancres, Exam. of	575
Cat's Hair, 857; Cat's Tail	856	Chandler on Iodinol Diag.	33
Caulophyllin, 1 to 4 gr.	848	Chanvre Indien...	266
Caustic. <i>Mitigated and Tough</i>	175	Chaparro Amargosa	849
,, Barii	221	Charbon Naphtholé, 60 to 120
,, Zinci Chloridi	827	gr.	571

FIGURES IN HEAVY TYPE, *e.g.* 199, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Charcoal (Animal, Wood) ...		846	Chloratitric ...		711
Charta Sinapis (Sinapizata) ...		763	Chlorazene ...		51
Chatin and Goitre ...		714, 425	Chlorazol Blue, 3B. ...		191
Chaulmartin ...		609	Chlorbutol ...		248
Chaulmoogrates ...		607	Chlorcosane ...		53
Recent Clinical Trials with		609	Chloretone, 5 to 24 gr. ...		248, 220
Chaulmoogra Esters ...		609	Inhalant ...		248
Chaulmoogra Oil, 5-10 m. ...		605	Chlorhydrate d' Amyleine ...		350
Ointment ...		607	Chloric Ether, 30 to 40 m., or 5		
Cheatles' Green Spray ...		324	to 20 rep. ...		290
Cheatle's Paste ...		462	Chlorides as Impurity Estn. 152, 153		
Chebulic Myrobalans ...		855	Titration ...		192
Cheese, 589; Chekan ...		850	Chlorine as Antiseptic... ..		270
Cheiranthus Cheiri ...		850	Ionisation ...		238
Chelidonium Majus ...		850	Chlorinated Eucalyptol ...		53
Chelsea Pensioner, 1 to 2 dr. ...		797	Paraffin (Liquid &		
Chemical Food, $\frac{1}{2}$ -2 dr. ...		418	Hard) ...		53
Chemotherapy ...		195, 39	Chlorine, Poisoning by ...		1101
Index ...		195	Chlorine Treatment of Scabies,		
Chenopodium ...		850	see Scabies Therap. Index.		
Cheratina ...		697	in Water ...		432
Cheron's Serum ...		769	(See also Water.)		
Cherry Bark, Wild ...		878	Chlorobrom, $\frac{1}{2}$ to 1 oz. ...		284
Cherry Laurel Water ...		151	Chlorodyne (Caps., 5 m.), 5 to		
Chestnut (Horse) ...		835	15 m. ...		290, 627
Chewing Gum Coca ...		332, 850	Recommendation as to		
Chian Turpentine ...		890	Strength ...		1014
Chicken Ess., Peptones ...		582	Chloroform, 1 to 5 m. 284 & 58, 271		
Jelly ...		639	Dangers ...		286
Pox and Small Pox 953, 996			and Ether Anæsthetic ...		288
Chicle ...		850	c. Ethyl Iodide, Sterules		112
Chicory ...		757	Inhalers ...		285
Chiendent ...		506	Oxygen-Anæsthesia ...		286
Chilblains. ...		1045	Sickness ...		286
Childbirth, Gwathmey's Method			Sterules, 10, 20, 30, 60 m.,		
(See also Twilight Sleep) ...		107	and G., 5 m. ...		289
Chillie Paste (Smedley's) ...		273	Chloroform, Aconiti, 1 in 1 ...		98
Chillprufe. ...		762	Camphorat ...		289
China Clay, 143; Root ...		858	Iodi, 1 in 30 ...		512
Chineonal, 10 gr. ...		820	Mastiche ...		289
Chinese Almond, 841: Ink 576, 577			Chloro Mercury Fluorescein ...		490
Chinina, etc., <i>vide</i> Quinine ...			Chloromorphiæ Liquor, 5 to		
Chinoform, 1 to 5 gr. ...		727	15 m. ...		290
Chinolini Tart., 5 to 15 gr. ...		316	Chlorophenols ...		21, 271
Chinolinum, 3 to 10 m. ...		316, 218	Chlorophyll ...		851
Chinosol, 1 to 5 gr. ...		316, 729, 218	Chloro-Sodio-Mag. Aper., 1 dr.		
Gauze ...		317	or more ...		780
Chirata, 851; Japanese ...		851	Chloryl Anæsthetic ...		110
Chlor-Sparklet Apparatus ...		432	Chocolate ...		804, 163
Chloral Caffeine hyp. 3-8 gr. ...		252	Culture Medium ...		911, 618
Camph. (et c. Cocain) ...		282	Cholagogues ...		1048
c. Menthol, c. Phenol,			Cholecystitis ...		451
et c. Thymol ...		556	Cholecystitis, Hexamine 100 gr.		
Formamidum, 15 to 45			doses in ...		681
gr. ...		283	Cholecystography ...		680
Hair Stimulant ...		283	Cholera, 913; Mixtures, 383,		
Hydras, 5-20 gr. ...		282, 220	1046; Treatment, 769; Vac-		
Tannin ...		283	cines, 913, 949; Vibrio 913 & 439		
Chloralamid. 15 to 45 gr. ...		283, 218	Cholesterol ...		101, 104, 105, 368
Chloralamide and Diphenyl-			For Syph. Test ...		580
amine Pastilles ...		318	Cholesterol and Vitamin D. ...		594
Chloramine-T., 51, 9, 220, 432;			in Blood ...		385
Bact. Power, 52, 9; Gauze,			in Urine ...		384
52; Ointment, 52; and Tabs,			Choline ...		5, 394
8-75 and 43-75 grains ...		52			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Choline Borate Solution, 3 to 20 Cc. dil	5	Cineol, 1 to 4 m.	614, 1299
„ Hydrochlor, 0.6 Gm. intrav.	5	Cinnabar=Red Mercuric Sulphide	4777
„ stearo-glyceroph., 3 to 5 gr....	...	539, 90	Cinnaldehydum (Cinnamal), 1 m.	26, 60, 2200
Cholumbrin	679	Cinnamoyl-oxyphenyl Urea... 8244	...	8244
Chondrodendron toment.	876	<i>Cinnamomi</i> Cort., 10-30 gr. 298, 600	...	298, 600
Chondrus	851	Cinnamon Paste, Dental 298, 509	...	298, 509
Chriminaline	655	Cinnamon, Wild	8455
Christmas Rose...	893	Cinnamyl Cinnamate	8883
Christopherson's Bilharzia Treatment	162	Cinnnoxyl Caps.	3122
Chromic Anhydride	832	Cinyl Alcohol	8041
„ Catgut (Lister)	541	Cirio de Flor. May.	8499
Chromii Sulphas	541	Citral	1266
Chromo-santonin, 2 to 5 gr.	760	Citrated Milk	586, 7733
Chrymotherapy	22	„ Media...	6183
<i>Chrysarobinum</i> , $\frac{1}{2}$ to $\frac{1}{2}$ gr. 294, 220	...	294, 220	Citrine Ointment	4663
Chrysarobin Acetates	295	Citronellæ Oleum	1299
Chrysoidine	326	Citronellol	1299
Churchill's Iodine	516	Citronenol	1322
Chyluria	380	<i>Citrus</i> var.	8422
Chymosin	76	Claret	266
Cibalgin	331	Clarke's Blood Mixture	6277
Cibrola	37	„ Soap Solution	4200
Cicatricine, 8 to 15 m....	...	765	Claudius' Iodine Solution	5411
Cicfa	632	Clayton Gas	183
Cicuta, F.E. = Conine; C. <i>Virosa</i> 851	...	851	Cleaver's Grass	8583
Cicutine, $\frac{1}{2}$ to 2 gr.	381	Clemens' Solution, 1 to 5 m.	1811
Cider	26, 493	Cloud-berry	8322
Cigarettes, 873; Asthma, 717; Cubebs, 852; d'Espic	717	Cloudy Ammonia	1493
Cigue	381	Cloves, 847; Clubmoss Spores 8688	...	8688
<i>Cimex</i> Var.	553	Coagulant Hæmostatics	9744
Cimicifugæ Rhizoma, 15 gr.	851	Coagulen Ciba	9744
Cimicifugin, 1 to 6 gr.	851, 220	Coagulose	9744
Cimolite	143	Coal Gas, poisoning, <i>see</i> Carbon Monoxide	1101
Cina	759	„ Tar Derivatives	299 & 600
Cinchona Calisaya, 'gray,' Lancif., Officinalis, etc. 295 & 59	...	295 & 59	„ „ Disinfectants, 30, <i>et seq.</i> & 2644	...	299 & 600
Cinchona Ledger.	155, 157	„ „ Inhaler and Vaporiser 2999	...	2999
Cinchona Febrifuge	719, 720, 155	„ „ Soap	7611
Cinchona Cultivation	296 & 155	Cobra Venom	9600
„ Robusta	157	Coca Chewing Gum	3322
<i>Cinchonæ Succirubræ</i> Cort., 5 to 60 gr.	296	Cocæ Folia. 30 to 120 gr. 331 & 65	...	331 & 65
„ Alkaloids, Tests	155	„ „ History of	3311
Cinchonidine	719, 723, 220	<i>Cocaina</i> , 1/20 to $\frac{1}{2}$ gr.	3333
„ Bismuth Iodide, $\frac{1}{2}$ to 1 gr.	230	Tests, Manufacture	65, 2201
„ HCl. (& Ac.), 1 to 10 gr.	723	<i>Cocaina</i> c. Oleo 2%	3355
„ Salicyl., 5 gr.	724	<i>Cocaina</i> Carbolas	3400
„ Sulph., 1 to 10 gr. 723, 271	...	723, 271	„ Citras, Formas	3355
„ Periodide, 1 $\frac{1}{2}$ to 3 gr.	135, 723	„ HI, HBr.	3400
Cinchonina and HCl. and Ac. HCl., 1 to 10 gr. 719, 724, 220	...	719, 724, 220	„ <i>Hydrochlor</i> , ($\frac{1}{10}$ to $\frac{1}{2}$ gr. B.P.'14	...	336, 67, 2201
„ Sulph., 1-10 gr....	...	724	„ Lactas	$\frac{1}{20}$ to 3400
„ Sulphocarb.	724	„ Nitras	$\frac{1}{2}$ gr. 3400
Cinchophen, 8 to 15 gr.	317	„ Nitris	3400
Cinematography X-ray	294	„ Phenas	3400
			„ Salicyl	3400
			„ Sulph.	3400
			Cocaine 'Activated'	132
			„ Abuse of	333
			„ Antidotes	334
			„ Dental Use	336, 1003
			„ Dusting Pdr.	343

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Cocaine Eye Drops (Factory Act) ...	335, 1011		Codliver...	618
„ Eye Lotion, Isotonic. ...	338		Coenzymes	77
„ in Clove Oil	334		Cofectant	32, 264
„ Ionisation	285		Coffee	51
„ Lanoline	334		„ De-cafeinated	51
„ Local Infilt. Anæsthesia c. ...	342		Cognac	118 & 26	
„ Lumbar puncture	343		Cohen's Salicyl Mist. 1 to 2 dr. ...	67	
„ Menthol-Eugenol	334		Cohosh, Black, 851; Blue	848	
„ Menthol-Phenol	334		Coke F., on Skin Tests 668 <i>et seq.</i>		
„ Oleate	335		„ Asthma Treatment	671	
„ Perforation of Septum	67		„ Oven Oils	30	
„ Periodide, 1/40 to 1/20 gr. incr. ...	135, 340		Cola Acuminata	248	
„ Pharmacology of	69		Colalin Tabs., $\frac{1}{2}$ to $\frac{1}{2}$ gr.; Colalin Laxative	783	
„ Poisoning	334		Colchici Cormus, 2 to 4 gr.	357 & 69	
„ Purification of	66		„ Semina, 3 gr.	357 & 69	
„ Salts incompat. c. Sod. Bicarb. ...	132		Colchicine, 1/100 to 1/32 gr.	358, 220	
„ Sniffing	333		„ Salicyl. (Caps. $\frac{1}{250}$ gr.)	359, 220	
„ Sterilisation of Sols.	338		Colchisal	359	
„ Substitutes	343, 69		Colcothar	93	
„ Synthetic	333		Cold Cream	876	
„ Tests for	66, 220		„ Vaccine, 908; <i>See also</i>	1044	
„ for Tooth Extraction	336		Cole Maclean Method	496	
„ Toxicology	65		Cole and Onslow's Broth	606	
„ Unrestricted Sale of	997		Coleman's Wincarnis	627	
„ Uses of	340		Coley's Fluid, claim for—B.M.J., i./28, 1134.		
„ versus Synthetics	342		Celic Root	837	
Cocculus Indicus	877		“COLLAPSES” OF OINTMENTS, <i>p.</i> 11:—		
Cocculus Diversifol.	851		† „ Aristol, 10%	510	
Coccus Cacti	846		* „ Atropine, 1 in 100, &c.	215	
Cochineal, Liquid, 847 (Indicator	187		* „ Atrop., 1% & Cocain. 2%	215	
Cochlearia Armoracia	852		* „ Atrop., 1%, & Iodof... ..	215	
Cocillana, 851; Cockle's Pills	627		* „ Atropine, 0.5% c.	215	
Cock's comb, Ergot assay	77		„ Ung. Hyd. Ox. Flav.	215	
Cocoa, 804 & 163; Food	586		\$ „ Bism., Morph. Coc.	228	
„ Nut Charcoal	846		„ Bism. Subgallate	237	
„ Nut Oil, Shampoo, Stearin and Soap ...	91, 92		* „ Boric Acid Oint.	11	
Col Liver Oil, 1 to 4 dr.	616, 133		* „ Boric Acid in White Petroleum Jelly, 1 in 60	11	
„ „ Emulsions	617		„ Boric Cream	11	
„ „ Substitutes	619		**†\$ „ „ Petroleum Jelly	11	
„ „ and Rickets	595, 99, 105		† „ Dermatol, 10%	237	
„ „ Vitamin Concentrates	618		\$ „ Ferri Perchlor.	413	
Codeina, $\frac{1}{4}$ to 2 grains	355, 139		\$ „ Gall and Opium	631	
Codeine Glycerin Jelly. 1 dr.	355		\$ „ Hamam. (et c. Codeina)	449	
Codeinæ HBr., $\frac{1}{4}$ to 2 gr.	356		* „ Homatropine and Codeina, ea. 2%	463	
Codeinæ HCl., $\frac{1}{4}$ to 2 gr.	356, 220		† „ Hyd. Iodid, 1%	473	
„ Periodid., $\frac{1}{4}$ gr.	135, 356		„ Hydrarg. Salicyl.	473	
Codeinæ Phosphas, $\frac{1}{4}$ –1 gr.	357		„ Hydrastis (5% Liquid Extract).	509	
„ Sulph., av. $\frac{1}{2}$ gr.	357		**†\$ „ Iodoform, 5%, et Codeina, 2%	509	
Codeine-Sodium Diethylbarbiturate, 5 gr.	569		† „ Iodoform, et Eucalypt., 5%	509	
Codeine Methyl-Brom., $\frac{1}{4}$ gr.	567				
Codeonal, 5 grains	569				

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FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
"COLLAPSUBES" OF OINT- MENTS—<i>ctd.</i> :—			Colloidal Patents on	366
† „	Iodol, 5%, et Euca-	510	„	Physiological Expts.	371, 372, 374, 375, 377
†§** „	Lanolin & L. Cream...	—	„	Solutions, Aluminium	369, 377
„	Lubric. Jelly ...	430	„	„ Antimony	365, 366
* „	Methysal Balm ...	72	„	„ Arsenic	365, 366
* „	Pagenstecher's, 1.25	476	„	„ Bismuth	365, 377
„	to 10% ...	654	„	„ Calcium	377
„	Paraffin, Soft ...	654	„	„ Copper (1 in 2000)	377
„	Petroleum Cerate ...	63	„	„ Gold (1 in 4000)	377
† „	Picric Acid, ½% ...	177	„	„ Test in C.S.Fluid	400
† „	Silver Proteinat ...	16	„	„ Iodine ...	371, 277
„	Surgical Lubricant ...	—	„	„ Iron ...	377
** „	Tannin, 10% ...	458	„	„ Lead ...	377
„	Ung. Prophylaxis ...	556	„	„ Lead Iodide	374, 1044
† „	Zinc Permang., 1 in 2000	831	„	„ Lead Selenide	374, 1044
† „	Zinc Sulph., 1 in 500...	—	„	„ Manganese	377
† „	Zinc Sulphocarb., 1 in	—	„	„ Mercury (1 in 2000)	377
	500 ...	—	„	„ Palladium	377
Collargol (Colloid Silver)	176, 220, 577		„	„ Platinum (1 in	4000) ...
Collinsonia Canadensis	852	„	„ Protective for .	366
Collip's Parathyroid ...	993		„	„ Selenium (1 in	5000) ...
Collobell preps. 369, 370,	372		„	„ Silver (1 in 2000)	377
<i>Collodium</i> (contractile)	...	359	„	„ (Collargol) ...	177
„ Acetonum ...	359		„	„ Sulphur (1 in	1000) .
„ Aceto-Æthericum ...	359		„	„ Verification & Tests	366
„ Anodynum ...	360		„	„ Therapy and Uses ...	366
„ Belladonnæ ...	224		Collosols, Argent, 377, 271; Hy-		
„ Benzoini ...	360		drarg, 377 <i>et seq.</i> ; Iodine,		
„ Callosum ...	360		372; Manganese, 374;		
„ Cantharidis (var.)...	269		Selenium, 376; Sulphur ...		377
„ Cocainæ, 2% ...	335		Collunarium Alum, T.H., 1%		
„ c. Ol. Crotonis, 1 in 7	360		„ Pot. Permang., Liq.,		—
„ Elasticum ...	360		6 m. in 1 oz., T.H.		—
„ <i>Flexile</i> ...	360		„ Potass. Chlorat Co.		777
„ Ichthosulphol ...	504		„ Quininæ ...		777
„ Iodi, 30 gr. in 1 oz.	360		„ Zinc. Sulph., 0.1%...		—
„ c. Iodoform. ...	508		„ Zinc Sulphocarb., 1		—
„ Kelly's ...	360		in 250 ...		—
„ Paraformi ...	132		Collutorium Acidi Benzoici ...		
„ 'Sacs' ...	403		„ Acidum ...		99
„ Salicyl ...	360		„ Alkalinum Co. ...		777
„ Salicyl. et Lact. .	360		„ Astringens ...		822
„ „ c. Hyd. Perchlor	360		„ Formalini ...		122
„ „ c. Zinc. ...	360		„ Hydrogen Perox. ...		498
„ Salol, 82; Styptic...	361		„ Pot. Permang. ...		555
„ <i>Vesicans</i> ...	269		Collyr. Adstring. Lut. ...		822
„ Zinci Chloridi ...	827		„ Horsti ...		822
Colloid Substances ...	281		„ Hyd. Biniodidi.		46
Colloidal Metals ...	361		<i>Colocynth. Pulpa</i> , 2 to 8 gr. ...		38
„ Antiseptic Powers	379 & 271		Colocynthin ...		38
„ Doses, <i>see</i> Individual			Colon Bacillus and Vaccine		92
„ Solutions in text.			Colonic Anæsthesia ...		160
„ Electric properties ...	363		Colostrum ...		40
„ Manufacture, Methods	365		Columbia Wax ...		33
„ Methods, published...	365		Colza Oil .		76
„ Author's Chemical ...	369		Comfrey .		88
„ Author's Electrical .	378				
„ Metal Organsols ...	380				

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FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Combined Cold Vaccine	...	908	Copper, Water Sterilism. with...	...	433
'Complement'	...	896	Copra	...	91
„ Deviation, Syph.	...	579	Cordite	...	575
Comp. Asthma Fluid	...	213	Coquelicot Fleurs de	...	625
Conarium	...	964	Corallin	...	189, 418
Condensed Milk	...	588	Coramine	...	265
Condurango, 15 to 60 gr.	...	852	Coriander	...	852
Condy's Fluids	...	555	Cordova's Modifd. Eusol	...	48
Conessine	...	536, 862	Corn Ergot and Silk	868, Oil,	619
Confectio Aromatica = Pulv. Cretæ	...	629	Corns, Collodions for	...	360
Aromatica, 10-60 gr.	...	629	Cornutine, $\frac{1}{2}$ to $\frac{1}{2}$ gr. <i>p.d.</i>	...	406
Confectio Glyceroph Co., 1 to 2 dr.	39	39	Coronilla	...	852
„ c. Malt, 1 to 2 dr.	...	797	Ceronium Bromide	...	788
„ Guaiaci Co., 1 dr.	...	658	Corpora Lutea, 5 to 10 gr.	...	959
„ Petrolei, 1 to 2 dr.	...	—	Corrosive Sublimate	...	171
„ Piperis, 60-120 gr.	...	882	Cortin	...	513
„ Rosæ Gal.	...	883	Coscinium, 845; Coster's Paste	...	852, 164
„ Rutæ, 1 to 2 dr.	...	760	Costus	...	573; Phthalate, $\frac{1}{2}$ gr. incr. 574, 222
„ Santonini Co., 1 dr.	...	—	Cotarnine HCl., $\frac{1}{4}$ to $\frac{1}{2}$ gr. incr.	...	382
„ Scammonia Co., '85,	...	886	Coto Cort., 1 to 8 gr.	...	383
10 to 30 gr.	...	886	Cotoin, $\frac{1}{2}$ to 2 gr.	...	435
„ Sennæ, 60-120 gr.	...	797	Cotton Medicated	...	443
„ et Piper.	...	—	„ Seed Ext. Pdr., 1 dr.	...	263
„ Sulphuris (et c. Senna)	...	506, 837	„ Oil	...	282
60 to 120 gr.	...	27	Couch Grass	...	29
„ Terebinthinæ, '85, 60	...	29, 222	Coulomb.	...	543
to 120 gr.	...	381 & 70, 222	Coumaric Treatment	...	851
Congo Red	3, 187, 413, 415, 579	381 & 70	Coumaric Anhyd.	...	952
Congreve's Elixir	...	627	Coumarin	...	253
Conii Folia and Fruits, 2 to	...	381 & 70, 222	Council mania dysenteria	...	377
8 gr.	...	381	Court Plaster, 863; Courtauld's	...	859
Conine, $\frac{1}{4}$ gr., incr.	...	606	Art Silk, 439; Cowbane	...	486
Coninæ HBr., HCl., $\frac{1}{2}$ gr. inc.	...	1048	Cowhage, 1 to 2 gr., 424; Cow-	...	487
Conjunctivitis	...	383	pox,	466
Conradi's Koleradraaber	...	1048	Crab's Eyes = Calcii Carb.	...	549
Conradi Drigalski Medium	...	729	Craie Préparée	...	486
Constipation	...	729	Cramer's Test	...	487
Contents	...	359	Cranesbill Root	...	480
Contraceptalene	...	799	Cream Artificial Act 1929	...	66
Contraceptives	...	800	„ Ice	...	718, 154
Contractile Collodion	...	852	„ Assay, etc.	...	248
Contramine Intram., 4 grains...	...	864	„ of Malt preparations	...	363
„ Intrav., 0.25 Gm.	...	292	„ Preservatives	...	176
in 10 Cc.	...	101	„ Reconstituted	...	66
Convallaria Majalis	...	869	„ Regulations	...	448
Convolvulus	...	391	„ Salicylic	...	462
Coolidge "X" ray tube	...	34	„ of Tartar (Soluble, 719).	...	458
Cooper's Weedicide stated to	...	286	20 to 60 gr.	...	546
contain 36% of Arsenious	...	601	Creams, Mpts. of	...	813
Oxide by weight. Inquest on	...	390, 831	Creatinin. Creatin	...	828
Mrs. Greenwood, June 16/20.	...	391	Crédé's Silver (Ung. 176), $\frac{1}{2}$ to	...	829
Coorchi, see Kurchi.	...	624, 137	2 gr.	...	205, 455
Copaiba, 30 to 60 m.	...	624	Crembas	...	66
„ Oil, 5 to 20 m.	...	624	Cremor Acid Salicyl	...	814
„ Resin	...	624	„ Emolliens	...	876
„ Soluble	...	869	„ Frigid	...	448
Opal Solution	...	391	„ Hamamelidis	...	462
Copper Alanin	...	370	„ Hyd. Zn. Cy.	...	458
„ Comps., Organic	...	34	„ Lowndes	...	546
„ Colloidal	...	286	„ Magnesiae, 1 to 4 dr.	...	813
„ Hair Dye	...	601	„ "Sicc" preparations	...	828
„ Ionisation	...	390, 831	„ Zinci	...	829
„ Oleate	...	391	„ et Calaminæ	...	205, 455
„ Points	...	391	Crec-Camph. Cream	...	205, 455
„ Sod. Tart.	...	391			

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Creocarb. Capsules	385	Cupri Oxidum	389
Creolin Pearson	32	„ Subacetat	389
Creophen	32	„ Sulphas., $\frac{1}{4}$ to $\frac{1}{2}$ gr.; emetic	...	389, 2711
Creosotal, 5 to 20 gr.	386	„ 5 to 10 gr.	389, 2711
Creosote Carbonate, 5-20 m.	386	„ Sulphocarbolas	199
„ Phenyl Propion. 10 m.	387	Cuprocyan	3911
„ Valer., 4 to 12 gr.	387	Cuprol	281
Creosoted Oil	659	Cuprum, 388 & 70; Alu-	...	
<i>Creosolum</i> , 1 to 5 m. incr., 383	...	383	minatum	390
		& 70, 271	“Cuprung”	389
Cresineol	130	Curara, $\frac{1}{20}$ th to $\frac{1}{2}$ gr.	853
<i>Cresol</i> , 1 to 3 m.	30 & 5	Curarina $\frac{1}{400}$ to $\frac{1}{40}$ gr.	853
Cresol-Soap Sola.	31	Curcuna Zedoaria	739
Cresoprine	91	Curdled Milk	58 & 100
Cresylic Disinfectants	32	Curdling Ferment	637
Cresyl hydrate	30	Curd Soap	760
Creta Gallica	144	Curic Wafers, 627; Curicones, 627	...	
„ <i>Preparata</i> , 15-60 gr.		<i>Cusso</i> , $\frac{1}{4}$ to $\frac{1}{2}$ oz.	
Crile's Anoci-Association	105, 499	Curschmann's Solution, 15 m.	264
Crile's Tube	286	Cusparia...	853
Cristolax	657	Cutaneous Tests	664
Crocus	852	Cutch, <i>see</i> Catechu nigrum	848
Cromessol	130	Cuticura	627
Crosby's Balsamic Elixir	627	Cyanamide	522
Crotalin, 960; Crotin	875	Cyanide Gauze, and Paste	436, 438
Croton-Chloral Hyd., 5 to 20 gr.	247	Cyanine Dyes	317
„ Eluteria	848	Cyanogen radical, effect of	255
„ Gubouga	875	Cyanuretum Hydrargyri	459
„ Tigllum	875	Cyclic Ureides	817
„ Elliottianus	875	Cyclohexanol	294
Cryogenin, 3 to 24 gr.	8, 222	Cydonia Semina	853
Cryptopine	139	Cyllin Preps., 1 to 5 m.	32, 264
Crystal Soda	772	Cymene, 541; Cyna	759
Crystal Violet	321 & 271, 599, 605	Cynips Gallæ	858
Crystalloids	361, 231	Cynodon	837
Cubeb Cigarettes	852	Cynoglossum	854
Cubebin	222	Cynotoxin	170
<i>Cubebæ Fruct.</i> , 30-60 gr.	623, 852	Cyperus Rotundus	854
Cuca, <i>see</i> Coca.	...		Cypress Oil	854
Cucumber Ointment	853	Cystamin, 5 to 15 gr.	450
<i>Cucurbitæ Semina Præp.</i> , 3 to	...		Cystazol Tabs., 1 to 3 in water	...	453
4 oz.	853, 876	Cystin	369
Cudbear	91	Cystitis, Mercurome in	...	482
Culex <i>var.</i>	553, 614	Cystoformin	454
Culture Media	617	Cystogen, 5 to 15 gr.	450
Cumene, Cumol	541	Cystopurin, 30 gr.	454
Cuprammonium Silk	440	Cytisine, 854; Cytisus Laburnum	...	854
Cuprase	370	Cytisus Scoparius	784
Cuprea Bark	387	Cytolysin	896
Cupreine and Comps.	387	Czapeck's Medium	493
Cuprentum	389			
Cupri Acet., 1-12 to $\frac{1}{2}$ gr.	389	Daccol Vaccines	942
„ Alanin	391	Dahlia	757
„ Alginas, $\frac{1}{24}$ to $\frac{1}{6}$ gr.	837	Daisy Powders	627
„ Alloxanæs	71	Dakin's Hypochlorite Solutions	...	49, 3, 2711
„ Amino-propionas	391	„ „ Daufresne's	...	
„ Ammon. Sulph....	...	390	Modfn.	50
„ Arsenis, $\frac{1}{100}$ th to $\frac{1}{25}$ th gr.	184	Dalby's Carminative	627
„ Aseptol	19	Dalmatian Flowers	880
„ Chloridum, $\frac{1}{4}$ to 2 gr.	390 & 271	Damaroids	627
„ Citras	389	Damiana	854
„ Glycinas	71	Dammar	854
„ Hippuras	71	Damson, Mountain	887
„ Nucleinas	281	Dandelion	890
„ Oleas	601			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE
DANGEROUS DRUGS:		
ACTS SUMMARY ... 1004		
1920 Act	...	1005
„ Appeal Case (Livpl.)	...	68
„ Castor Oil Cocaine for Factories	...	1011
„ S.R. & O's under <i>et seq.</i>	...	1006
„ Prescriptions, 1004, 1007; N.H.I.	...	1007
„ Marking of Packages	...	1008
„ Recent data	...	67
„ Records	...	1008
„ General Authorisations...	...	1009
„ Exempted products	1010, 1011	
„ Hospitals	...	1011
„ Nursing Homes	...	1011
„ Records Schedule	...	1010
„ Special Authorisations	1010, 1011	
„ Midwives	...	1012
„ Trade in	...	67
DANGEROUS DRUGS ACT, 1923,		
„ Amending [P] Sales	...	1012
„ 'Signed Orders'	...	1013
„ Percentages	...	1013
„ References	...	1015
„ Points of Assistance	...	1015
„ Supplies to Medical Men	1004	
D.D.A. CALCULATION TABLES 1017		
„ Examples of Scripts	...	1020
„ „ of Dentist's Scrip	...	1021
„ „ „ Vet-Surg's Scrip	...	1021
„ „ „ 'Signed Order'	...	1022
DANGEROUS DRUGS ACT,		
1925	...	1014, 68
D.D. REGULATIONS 1926 ... 1014		
Danish Glossary, 641; Ointment	...	799
Danistol Caps.	...	423
Danysz Method...	...	672
Daphne Mezereon	...	870
Datura var.	...	502, 787
<i>Datura Folia et Semina</i>	...	787
Daturine	...	787
Daufresne's Modifd. Dakin Soln.	...	50
Davis' Pills	...	628
Deadly Nightshade	...	222
Dearborn Preps.	...	628
Deba	...	817
Decalcified Dietary	...	257
Dechlorination	...	770
Decocta Concentrata	...	391
Dec. <i>Acacie Cort.</i> , $\frac{1}{2}$ to 2 oz.	...	832
„ <i>Agropyri</i> , $\frac{1}{2}$ to 2 oz.	...	837
„ <i>Aloes Co.</i> , $\frac{1}{2}$ to 2 oz.	...	137
„ <i>Apocyni</i> , $\frac{1}{2}$ to 1 oz.	...	170
„ <i>Cannabis Sativ.</i> , 1 oz.	...	845
„ <i>Cetrariae</i> , '85, <i>ad lib.</i>	...	849
„ <i>Chondri</i>	...	851
„ <i>Conchonae</i> , '85, 1 to 2 oz.	...	297
„ <i>Cydoniae</i>	...	854
„ <i>Eryngium</i> , 5 oz.	...	856
„ <i>Eucalypti</i> , 2 to 4 dr.	...	856
„ <i>Euphorbiae Pepli</i> , 1 tea- cup	...	857

NAME.	DOSE.	PAGE
Dec. <i>Granati Cort.</i> , B.P. '98, 1 in 5, $\frac{1}{2}$ to 2 oz.
„ <i>Hæmatoxyli</i> , $\frac{1}{2}$ to 2 oz.
„ <i>Ispaghulae</i> , $\frac{1}{2}$ to 2 oz.	...	864
„ <i>Levisticum</i> , 3 to 5 oz.	...	867
„ <i>Lin.</i>	...	867
„ <i>Papav.</i> (et <i>c.</i> <i>Anthem.</i>)...	...	625
„ <i>Paireira</i> , '85, 1 in 16, std. hot, 1 to 2 oz.
„ <i>Psylli</i> , <i>ad lib.</i>	...	879
„ <i>Sappen</i> , $\frac{1}{2}$ to 2 oz.	...	861
„ <i>Scoparii</i> and <i>Tarax.</i> , '85, 2 to 4 oz.
„ <i>Simarubæ</i> et <i>Granati</i> , 1 oz. 528, 536,	...	887
„ <i>Tritici</i> , $\frac{1}{2}$ to 2 oz....	...	837
„ <i>Ulmi</i> , 2 to 4 oz.	...	892
„ <i>Zittmanni F.</i> et <i>Mit.</i>	...	884
Deeks' Ointment	...	1051
Defatted Tuberc. Vacc.	...	942
DeLafield's Stn....	...	401
Delectol	...	657
Delhi Boil	...	552
Delphina, $\frac{1}{8}$ to $\frac{1}{4}$ gr.	...	888
Delphinium	...	888
Dengue Fever	...	614
Dental Anæsthetic, 10 to 25 m.	...	336
„ <i>Arsenical Fibre & Paste</i>	...	182
„ <i>Compo</i>	...	865
„ <i>Dressings, Sterile</i>	...	439
„ <i>Extractions</i>	...	337
„ <i>Fillings</i>	...	830
„ <i>Mastich</i>	...	869
„ <i>Paste, Cinnam.</i>	...	298
„ <i>Plasters</i> , 272; <i>Rubber</i>	270
„ <i>Solubes, Antiseptic</i> , 18; Wax	...	655
Dentifrice, Oxidising	...	496
Dentist's Scripts for [P] Drugs, <i>see</i> 1004 <i>et seq.</i> &	...	1008
Dentists Act	...	1023
Dentures, to clean	...	51
Depilatories	221, 261,	782
Derbyshire Neck,	714; &	
Therap. Index
Dermatitis	...	1051
Dermatol	...	236
Dermogen	...	496
Desensitisation	...	667
Desoxycholic Acid	...	783
Detoxicated Vaccines	...	901
Developer, Photographic	...	296
Devil's Milk	...	857
Dewees's Mixture, $\frac{1}{2}$ oz.	...	138
Dextrin	...	429, 369
Dextro-Pinene	...	148
Dextrose, 426, 222; Enema	...	402
Dhobie's Itch	...	1051, 534
Diabetic Foods, 591; Urines	...	370
Diabetin...	...	757
Diabetes, 1052, <i>see also</i> Insulin.
„ <i>Innoeens</i>	...	644
„ <i>Mell.</i> , Insulin in, 640 <i>et seq.</i>
„ <i>Prognosis</i>	...	647
„ <i>Drugs in</i>	...	647

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Diabetes, Operations in ...		648	Diffusol ...		32, 271
„ Pituitary in ...		647, 972	Digalen, 5 to 15 m. ...		400
„ Tests ...		370-373	Digestive Salt ...		770
Diacetyl-Amino-Azo Toluol ...		314	Digisol, max. 45 m. <i>p. os</i> ...		396
Diacetyldihydroxyphenyl-isatin ...		279	„ for Injection, max. 5 Cc. ...		396
<i>Diacetyl-Morphine HCl.</i> , $\frac{1}{25}$ to			Digistrophan Tablets ...		400
$\frac{1}{8}$ gr. ...		566, 139, 222	Digitalein ...		72
Diacetyl Tannin, 5 to 15 gr. ...		96	Digitaline, Cryst., $\frac{1}{250}$ to $\frac{1}{100}$ gr. ...		399
Diachylon Plaster ...		603	Digitaline, Amorphe, $\frac{1}{60}$ to $\frac{1}{30}$ gr. ...		399
Dial Tabs., $1\frac{1}{2}$ gr. Dose, $\frac{1}{2}$ to 3			Digitalinum, Nativelle gran-		
Tabs. ...		821 & 222	ules, $\frac{1}{240}$ & $\frac{1}{600}$ gr. ...		399
Dialacetin, $\frac{1}{2}$ to 1 tablet ...		822	„ Pulv. Pur., $\frac{1}{10}$ to $\frac{1}{2}$ gr. ...		400
Diamalt and with Oil ...		549	<i>Digitalis, Folia</i> , $\frac{1}{2}$ to 2 gr. ...		392 & 71
Diamide ...		31	„ Acetone Extractive ...		74
Diamido-azo-benzene HCl. ...		326	„ Assay ...		73
Diamidodiphenyl ...		393	„ Cat Unit Tablets ...		398
Diamidophenol HCl. = Amidol. ...		296	„ Cultivation, etc. ...		71
Diamino-Acridine Sulphate, 306 ;			„ Cumulative Action ...		395
HCl., 306 ; Patents, 306 ;			„ Flowers ...		74
Antiseptic Power, 306 ; Uses ...		306	„ Glucosides ...		398 & 72
Diaminothiobenzol ...		799	„ International Standard ...		75
Diamino-Methyl-Acridine Chlor. ...		305	„ Physiological Standardi-		
„ HCl. ...		300	sation 392, 396, 397 & 74		
<i>Diamorphine Hydrochloridum</i> ,			„ Preservation ...		71
1/25 to 1/8 gr., 566 ; and D.D.			„ Seeds ...		75
Restrictions ...		1005, 68, 639	Digitalone, hyp., 8 to 15 m. ...		396
Dia-Paraffin ...		549	Digitonin ...		72, 73
Diaphorm, 1/25 to 1/8 gr. ...		566	Digitoxin, $\frac{1}{250}$ to $\frac{1}{64}$ gr. (granules		
Diaplyte Vaccines ...		942	$\frac{1}{4}$ mgr.) ...		399 & 72, 73, 224
Diarrhoea Mixtures ...		383	Digitsaponin ...		72
Diascordium ...		890	Di-hydroxybenzene ...		750
Diaspirin ...		74	Di-hydroxy-hexyl Benzol ...		753
Diastase, Malt, <i>syn.</i> Maltine			Dihydroxyphenylethyl Methyl-		
„ Pancreatic ...		548 & 76, 93	amine ...		982
Diastasic Power, Expts. on ...		637	Dihydroxyphthalophenon ...		677
Diathermic Treatment ...		93	Di-iodo iso-propyl Alcohol ...		522
Diazo Reaction ...		313	Di-iodo-hydrin ...		522
Dibromfluorescein ...		611	<i>Dill Fruit</i> ...		840
Dibromin ...		399	Dilling. Prof. W. J., on Pro-		
Dibrom-malonyl-ureide ...		824	portional Dose ...		1108
Dibromo-oxy-Mercury-Fluores-			Dimethoxy Emetine ...		526
cein ...		824	Dimethyl-Amino-Antipyrin ...		330
Dichloramine-T... ...		479	„ „ Azo-Benzol ...		413, 415
„ in Eucalyptol ...		52, 224	„ -Amidobenzaldehyde ...		365
Dichlorbenzol <i>o</i> & <i>p.</i> ...		53	„ Benzol ...		312
Dichlorethylene ...		310	„ Carbinol ...		122
Dichlorethyl-sulphide ...		292	„ Ether ...		110
Dichloride of Ethylene. ...		1102, 500	„ -Ethyl-carbinol ...		839
Dick Test and Prophylaxis ...		292	„ Ethyl-carbinol, chloral ...		839
Dicodid ...		570	„ Glyoxime ...		166
Didial, 1 to 3 Tabs. ...		xxxvii	„ -Ketone, 1-1 $\frac{1}{2}$ dr. ...		832
Didymin ...		822	„ Meth-dieth. Sulphone. ...		795
Diet, Salt free, 770 ; Scale ...		983	„ Methoxyphenol ...		21
Dietary Defective ...		598	„ -oxy-quinizine ...		327
Dietetics ...		594	„ Xanthine ...		805, 807
Diethylamino propyl Cinnamate		581	Dimol Pulverettes, 2 to 4 ...		21
Diethyl Ammon.-Diethyl Di-		358	„ Preps ...		21, 22
thiocarbamate. ...		799	Dinitrobenzols ...		311
Diethyl barbituric Acid ...		817	Dinitro-cellulose ...		359
Diethylene-diamine, 4 to 10 gr. ...		702	Dinner Pills and Tablets ...		708
Di-ethyl Malonate ...		817	Diogen (developer <i>v.</i> P.J.I./07,429).		
Di-ethyl-malonyl-urea, 5 to 10 gr. ...		817	Dionin, $\frac{1}{4}$ to $\frac{1}{2}$ gr. ...		565
<i>Diethyl-sulfone-dimethyl-methane</i> ,			Di-ortho-Aminothio Benzene .		799
10 to 20 gr. ...		795	Diosal Sol. ...		72
			Dioxyanthraquinone ...		279

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Dioxydiamino-Arsenobenzol ...		194	Dormigene, 5 to 10 gr. ...		821
Diphenylamine ...		79, 420	Dormiol (Caps. 7½ m.) 5 to 50 m. ...		839
„ Eth-thymyl benz. ...		812	Dorset's Egg Medium ...		618
Diphenylcarbaid ...		490	Doses, Metric, and Imperial xxxviii.		
Diphtheria Antitoxin ...		915 & 537	„ Proportions acc. to age ...		1108
„ Anatoxin ...		538	Dose Table Intravenous ...		1106
„ Carriers ...		538	Douches, Contraceptive ...		729
„ 'Conc.' 916; Units			Dourine ...		586
„ B. Vaccine ...		917	<i>Dover's Powder</i> , 5 to 15 gr. ...		525
„ Endotoxin ...		540	Dowzard Process ...		137
„ Immunisation ...		538	Dracunculus ...		550
„ Infective Period ...		996	Drage's Investigations ...		26
„ Pigment for ...		413	Dragendorff's Test ...		49
„ Prophylactic ...		917, 538	Dragon's Blood ...		854
„ Schick Test for ...		538	Drainage Tubing ...		270
„ Toxin-Antitoxin 917, 538, 539			Dressings, Dental, 439; N.H.I.,		
„ Toxoid ...		539, 540	438; Sterilisation of, 438 &		
Diplo. Intracellularis ...		910	Vol. II; Steriloid, 437; Sur-		
„ Lanceolatus ...		566	gical 435; <i>et seq.</i> ; Preparation		
„ Neutral Red Medium for		927	of ...		438
„ Rheumaticus ...		927	Dreyer's Vaccine ...		942
„ Scarlatinae ...		574	Dried Milk ...		583
„ Still's ...		911	Dridustols ...		111
„ Weichselbaum ...		910	Drigalski-Conradi Medium ...		606
Diplosal, 15 gr. ...		73	Droitwich Brine Baths ...		456
Dipterocarpus ...		843	Drop Measure Tables ...		250
Diseases, Infective Periods		996	Dropwort ...		875
„ Index ...		1029	Drosera Rotundifolia ...		854
Disinfectants ...		30, 126, 552	Drug Addiction: Cannabis, 266,		
For storage of In-			627; Heroin, 567; Opium,		
struments—Thymol			627, 628. (<i>See also</i> Cocaine,		
Disinfectant.			Morphine, etc.). <i>All recent</i>		
„ Sale of ...		1000, 262	<i>data</i> ...		67, 68
„ Standardisation ...		262	Drugs, Dangerous, Acts 1004 <i>et seq.</i>		
„ Summary of Potent. ...		266	Dry Cleaning ...		276
Disinfection of Rooms 127, 131 & 13			Dryopteris ...		422
Disinfecter, "Formanganate" ...		128	Duboisia and Duboisine ...		210, 503
Dismenol ...		331	Ductless Glands, 175. <i>See</i> Glands		
Di-Sod. Methylarsen., $\frac{2}{5}$ to 3 gr. ...		188	in question.		
Disseminated Sclerosis and			Dugong Oil, 619; Dulcitol ...		606
T.A.B. Vaccine ...		951	Dulcin, $\frac{1}{2}$ grain ...		755
Distemper ...		923, 551	Dum Dum Fever—type of Kala-		
Distomiasis ...		275, 423	Azar ...		551
Dita Bark and Ditaine ...		838	Dunbar's Hay Fever Serum ...		919
Di-thymol-iodide ...		509	Dundas Grant's Inhalation Fluid ...		289
Di-Ureides ...		816	Dunham's Soln., 619: Tassel... Dunhill's Solution ...		414 347
Diuretic, the choice of a ...		393	Duodenal Membrane Tabs. and		
Diuretin, 10 to 20 gr. ...		805	Extract, 5 to 20 m. ...		960
„ Lithium, 5 to 15 gr. ...		806	„ Ulcer, 973 & Therap. Ind.		
Divi Divi ...		854	Duotal, 5 to 15 gr. ...		447
Dixon, Prof., on Opium Smok-			Duplitised Films X ray. ...		293
ing ...		627	Duralumin ...		142
Doan's Pills and Ointment ...		628	Durant's Injection ...		446
Dobell's Solution ...		772	Duret's Calomel		473, 82
Dochmiasis, <i>see</i> Ankylostom.			Durine ...		127
Dock, Yellow ...		883	Dusart's Syrup, 2 to 4 dr., 56; Wine ...		628
Dodd's Pills ...		628	Dust in relation to Asthma.		
Dog Grass ...		837	<i>See</i> Peptone Desensitisation.		667
Dogwood, Jamaica ...		493, 878	Dusting Powders, Formosyl		130
Dolichos Pubes ...		424	(<i>See also</i> 142, 829)		
Dols Flannel ...		350	Dutch Drops, 702; Glossary ...		642
Donovan's Sol., 5 to 20 m. ...		183	Duty-free Alcohol ...		122
"Dope" ...		443	Dye Excretion Tests ...		62, 63, 386
Doremus Ureometer ...		387			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Dyed Fur	308, 1051	EFFERVESCENT SALTS — <i>contd.</i>		
Dyer's Madder	832	Magnesium Citrate, 1-2 dr. or <i>q.s.</i>		
Dyes, Aniline, 300; as Anti-septics, 265; for foods	495	<i>Sulphate</i> , $\frac{1}{2}$ -1 oz....	5488	
(see also Individual Colors).			Phenacetin, 5 and 10 gr. ...	3239	
Dysentery, 917, 1054; Ana-toxin, 544; Serum (Bacilli) 917, 541			" 5% et Caffeine, $2\frac{1}{2}\%$...	3277	
" Auremetine in...	537	Phenolphthalein, $\frac{1}{10}$ to 2 dr.	678	
" Vaccine, 50 to 2,000 mill.	918		Pilocarpine, $\frac{1}{10}$ gr. ...	6966	
" Amœbæ, Search for	541		Piperazin, 5 gr. (et c. Pheno-coll) ...	7033	
" Treatment	526 et seq.		Piperidine Tart., 5 gr. ...	7033	
" Ipecac.	524		Potass. Citrate, 1 or 2 dr. ...	7177	
" Carriers, 528, 1055, 544; Treatment with E.P.I.	532		Potassic Aperient, et c. Pot. Sulphocarb. ...	7266	
'E 107'	246	Quin. Citrate, 1 gr. ...	7266	
E.M.F.	282	" Salicyl., 3 gr. ...	7355	
Eade's Pills	628	" Sulphate, 2 gr. ...	7399	
'E.P.I.', 2 grs.	532	Sal Bromatum	7711	
Ear Cones, 218; Cocaine	337	Salicin, 5 gr.	800	
Earth Nut Oil	841	Sodio-Mag. Aper. (et c. Caff-ein, 780)	7800	
Easton's Syrup (also Pills and Tablets, 420), $\frac{1}{2}$ to 1 dr.	419	Sodium Benzoate, 6 gr. in dr.	88	
Eau d' Alibour	390	" <i>Citro-Tart.</i> , 1 or 2 dr.		
In syccosis barbæ.—Ingram, B.M.J. ii./29, 620.			Sodium Phosphate, 1 to 3 dr.	7777	
Eau de Botot	840	" Salicyl., 5, 10 grs. ...	700	
" de Cologne	118	" Sulphate, 1 dr. or more	7800	
" de Goudron, 5-10 oz.	703	Stront. Brom., 10 gr..	7899	
" de Javelle	46	Sulphonal, 5 gr.	7955	
" de Labarraque	45	Tycalsin, 5 gr..	788	
" de Paris	118	Tyllithin, 5 gr.	799	
" de Melisse des Carmes	870	Vesalvine, 5 gr.	4522	
" Oxygénée	493	Egg Medium, 618; Yellow ...	4977	
" Sedative	263	Eggs, Dried, 494; Liquid ...	4944	
Ecbalium Elaterium	855	Ehrlich's Diazo Reaction ...	6111	
Ecgonine Derivs. 333 & 1005, 65, 67			" Ehrlich-Hata "	1944	
Echitamine	833	Ehrlich Stains and Tests ...	4011	
Echium	855	" Theory... ..	2511	
Ethol, 1 dr. well diluted	892	Ekatantalum	3311	
Eczema Marginat, Therap. Ind. 570			Ektogan	4963	
Eczoline Preps.	628	El Kossam	8444	
Edestin	443, 418	Elæosacchara, P.G. (<i>q.v.</i>).		
Edington's Soln.	336	Elarson Tabs.	1899	
Edmunds' Cell	32, 47	Elastica	2700	
EFFERVESCENT SALTS.			Elaterium, 1-40 to 1-10 gr.	855, 2244	
("gr." in drachm understood —dose, 1 dr. or <i>q.s.</i>):			Elaterium, 1-10 to $\frac{1}{2}$ gr. ...	855	
Acetanilide, 1 and 3 gr.	3	Elbon-Ciba, 30 to 60 grs. pro die ...	8244	
Ammon. Brom., 5 gr.	145	Elderberry Flowers	883	
Antipyrine, 5, 10, 15 gr.	328	Elecampane	863	
Bath Salts	779	Electrargol	3794	
Caffeine Citr. $2\frac{1}{2}$ gr. and c. Pot. Brom., 5 gr....	250		Electrocuprol	3784	
" HBr., $2\frac{1}{2}$ gr.	250		Electric Current Injuries ...	1105, 3111	
Carlsbad Salt (Vescettes) ...	780		" Shock	1105, 3111	
Catha Phenolphthalein, 1 to 2 dr.	848	Electricity, Medical	2792	
Chloro-Sodio-Mag. Aper. ...	780		Electrochemical equivalent ...	2366	
Glyceroph., 60 grs.	39		Electrolux Apparatus	4855	
Iron & Quin. Citr., 3 gr. ...	726		Electrolytes	2792	
Lecithin, 3 gr.	540		Electrolysis	2832	
Lithium Citrate	543		Electrolytic Solution pressure...	2792	
" Hippuras, 5 gr.	543		Electromotive Force	2822	
" Salicyl, 2 gr.	543		Electuaire Diascord., 15 gr. ...	890	
			Elements, Table of	xxxvi	
			Elephantiasis, see Filariasis Therap. Ind. & 545		

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
<i>Elettaria Cardam.</i>	846	Elixir Rhei, 1 to 3 dr.	401
Elimination Tests	355	„ Rubrum, 20-60 m.	401
Elixirs	401	„ Saccharini, 5 to 20 m.	755
Elixir Acetanilid. Co., $\frac{1}{2}$ to 1 dr.		3	„ Secretogen, 1 to 2 dr.	961
„ Acidi Salicyl. Co., 1 to 2 dr.	66	„ Sennæ (et Legum.), 1 to 3 dr.	886
„ Agrimonie Co., 1 dr.	837	„ Simplex, 20-60 m.	401
„ Aletridis, $\frac{1}{2}$ to 1 dr.	837	„ Sodii Brom-aceto salicylat., $\frac{1}{2}$ oz. rep.	76
„ Ammon. Brom., 1 to 2 dr.	145	„ Sodii Cacodyl, 30 m.	187
„ Antineuralg., 1-2 dr.	249	„ „ Formatis, 2 dr.	35
„ Aperitive, $\frac{1}{2}$ to 1 dr.	138	„ „ Lact., 1 dr.	57
„ Aromat., $\frac{1}{2}$ to 2 dr.	401	„ Symphyti, $\frac{1}{2}$ to 2 dr.	889
„ Arsamin ($\frac{1}{2}$ gr.), 1 dr.	190	„ Three Gland, 1 to 2 dr.	989
„ Aurantii Amari, 2 to 4 dr.	401	„ Thymi et Diaphorm, 1 dr.	892
„ Berberinæ, 1 to 4 dr.	844	„ Valerianæ et Bromidi, $\frac{1}{2}$ oz.	826
„ Bismuthi, 60 m.	230	„ Vanillin Co., $\frac{1}{2}$ to 1 dr.	893
„ Caffeinæ, 1 to 2 dr.	249	„ Vesalvine 'S', 1 dr.	453
„ Calc. Chlor., 1-2 dr.	258	„ Viburn. Prunif. (& Co.)	894
„ „ Iodidi, 1 dr.	259	„ of Vitriol, 5-20 m.	92
„ Camph., 30 to 60 m.	263	Elliman's	623
„ „ Monobr., 4 dr.	265	Elm	892
„ Cascara, 30-120 m.	277	Elschnig's Medium	566, 619
„ Chloralamidi, 1 oz.	234	Elsner's Reagent	440
„ Cinchonæ, 30 to 60 m.	297	Embalming	620
„ Cinchonidine, $\frac{1}{2}$ oz.	723	Embalment of Wounds	508
„ Coca, 1 to 4 dr.	332	<i>Embelia</i> , 1 to 4 dr.	855
„ Creosoti, 1 to 2 dr.	384	Emblie Myrobalans, 1 or 2	855
„ Curacao, 2 to 4 dr.	401	Emery's Method	263
„ Duodenalis, $\frac{1}{2}$ oz.	961	Emetamine	538
„ Ergotæ cum Ferro, 2 dr.	405	Emetina (Alk.)	525 & 224	
„ Ferri Phosph., c. Quin et Strych., $\frac{1}{2}$ to 1 dr.	420	„ HBr. Hyp., $\frac{1}{2}$ to $\frac{2}{3}$ gr.	531
„ Ferro-Mang. Pept., 1 to 4 dr.	416	„ HCl. Expect. $\frac{1}{100}$ to $\frac{1}{25}$ gr.	526
„ Ficorum, 1 to 4 dr.	401	„ „ Hyp., $\frac{1}{2}$ to $\frac{2}{3}$ gr.	529
„ Formatum, Co., 1 to 2 dr.	36	„ for Liver abscess	529
„ Four Gland, 1 to 2 dr.	989	„ Oleate, $\frac{1}{4}$ gr.	536
„ Gentian Ac., 1 to 2 dr.	859	„ Panama Bismuth, with ...	528, 537	
„ Glusidi, 5 to 20 m.	755	„ Periodide, $\frac{1}{2}$ to 2 grs. 135, ...	532	
„ Glyceroph, 1 to 4 dr.	39	„ „ in Dried Milk	533
„ „ c. Format., 1-2 dr.	40	„ „ Slipules, 2 gr.	532
„ Guaiaci, 1 to 2 dr.	445	„ „ Discussion on paper	535
„ Hæmoglobin, 1 dr. or more	583	„ „ Steriloids	134
„ „ c. Lecithin, 1 to 2 dr.	583	Emetin (Extractive) Expect $\frac{1}{16}$ to $\frac{1}{100}$, Emetic, $\frac{1}{2}$ to 1 gr.	539
„ Heroin, Pini et Terpin, 1 dr.	701	Emetine and Amœbæ 526 <i>et seq.</i> 39	...	
„ Ipecacuanhæ, 10 to 30 m.	524	„ Cumulative effect	39
„ Lecithin, 2 dr.	540	„ Bismuth Iodide, 1 to 3 gr. ...	531 & 224	
„ Lith. Hydrangea, 1 to 2 dr.	862	„ „ Diarrhœa	532
„ Manaca Salicyl, 1 to 2 dr.	868	Emetique, Max. single, 3 grains	161
„ Papain, 1 dr.	652	Emetol, 2 dr.	535
„ Paraldehyde, 1 to 3 dr.	126	Emodin	858, 886
„ Parathyroid, with Calc. Lact., 1 dr.	994	Empirin, 5 to 15 gr.	74
„ Paregoric, $\frac{1}{2}$ to 1 dr.	630	Emplast. Ac. Salicyl. Sap.	66
„ Pectorale, 1 dr.	860	<i>Emplast Adhesivum.</i>	603
„ Pepsin, Bism., Strych., 1 dr.	663	„ „ Ang.	863
„ Pepticus, $\frac{1}{2}$ oz.	662	„ „ Allii	838
„ Phosphori, 15-60 m.	688	„ „ <i>Belladonnæ</i> , 224; U.S. ...	224	
„ Pini et Terpin Sim., 1 dr.	701	„ „ Extensum	224
„ Pini, Terpin et Heroin, 1 dr.	701	„ „ <i>Calēfaciens</i>	268
„ Quinque Brom., 1 dr.	711	„ „ <i>Cantharidini</i>	268
„ Quinidine, $\frac{1}{2}$ oz.	722	„ „ <i>Cantharidis Liq.</i>	269
„ „ et Cinchon, $\frac{1}{2}$ oz.	723	„ „ <i>Capsici</i> (various)	272

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Emplast. Cocainæ	335	Emuls. Sevi	597
„ Cupri Oleatis	602	„ Sulphuris	927
„ Diachylon	603	Enamels Cellulose	442
„ Hydrarg. Stearatis	603	Encephalitis, Epidemic (lethargica) ...	1057,	545
„ Menthol.	557	„ Post Vaccinal...	545
„ Mouches de Milan (Emplatre)	268	Endocarditis Serum	928
„ Opii	629	Endocrine Glands	957
„ Picis	704	Endolytic Tubes 360, 364, 374,	400	
„ Plumbi	603	Endo's Medium...	608
„ Resinæ	603	Endotoxins	896
„ Saponis	603	Enemata	402
„ Vesicans	268	Enema, Acid Salicyl. 0·3%	403
Emulsifiers	583	„ Alum, 0·5%	403
Emulsin	151, 76	„ Ammoniaë	148
Emuls. Acriflavine	304	„ Aperiens	402
„ Agar. c. Paraff. Liq., $\frac{1}{2}$ to 1 ounce, children 1 to 2 dr.	658	„ Argent. Nit., 0·1%	403
„ Amygdalæ, av. 4 oz.	152	„ Asafœtidæ, 5% ...	403,	842
„ Asafœtidæ, 4 dr.	842	„ Barii Sulphatis	222
„ Barii et Bism.	222	„ Bismuth Carb. or Subnit., 1%	403
„ Benzyl Benz., $\frac{1}{2}$ to 2 dr.	312	„ „ Sod. Salicyl., 1 pint	235
„ Bismuthi et Paraffini, 1 oz.	657	„ Boric Acid. Sat. Sol.	403
„ Butol	598	„ Chloral, 4 oz.	283
„ Chloroformi	291	„ Dextrose	402
„ Iodinol, 2 dr.	520	„ Evacuans...	402
„ Iodoformi	508	„ Ferri Chloridi (Liq.), 2%	403
„ Lecithin, $\frac{1}{2}$ oz.	540	„ Glucose	402
„ Ol. Arachis c. Glucose...	841	„ Glycerin, $\frac{1}{2}$ oz.	402
„ „ Chaulmoogræ, $\frac{1}{2}$ to 1 dr.	606	„ Hyd. Perchlor., 0·01 to 0·05%	403
„ „ Gynocardii, $\frac{1}{2}$ to 1 dr.	606	„ Inf. Allii	403
„ „ Morrhuæ, 2 to 8 dr.	617	„ Lith Aceto-Salicyl c. Sod. Brom.	79
„ „ „ Ferrat., 2 to 8 dr.	617	„ Mag. Sulph., $\frac{1}{2}$ to 2 oz	548
„ „ c. Lecithin, 2 to 8 dr.	617	„ Mucilaginis, 25%	403
„ „ Morrhuæ et Glyceroph., 2 to 8 dr.	40	„ Nutriens	402
„ „ Morrhuæ et Hypoph., 2 to 8 dr.	617	„ Olei Ricini	621
„ „ Morrh. et Iodoform, 2 to 8 dr.	617	„ Olei Terebinth., 0·5 to 1% ...	403,	700
„ „ Olivæ. 1 to 2 oz.	620	„ Oleosum	620
„ „ Papaveris, $\frac{1}{2}$ to 1 oz.	619	„ Opii ...	402,	403
„ „ Paraffin c. Agar, $\frac{1}{2}$ to 1 oz.	658	„ Plumbi Acet., 1%	403
„ „ „ „ c. Phenolphthalein, $\frac{1}{2}$ to 1 ounce	658	„ Quinin Alcohol-Ether	108
(See also C. D. June 16'28 for a formula with Gelatin).			„ Rutæ	883
„ „ Paraffini et Bismuth 1 oz.	657	„ Sedativum, 5 oz. dilted...	79
„ „ Paraffin c. Pancreatino	656	„ Silver Gelatose	178
„ „ c. Rhamni Frang.,	657	„ Simplex	402
„ „ Petrolei c. Hypoph., 1 to 4 dr....	...	656	„ Sodii Chloridi	769
„ „ Terebinth., 1 dr.	700	„ Stimulant, for Thirst, etc. ...	402,	403
„ Salol, $\frac{1}{2}$ to 1 oz.	82	„ Tannin, 1%	403
„ Santonin	759	Energen Bread	112
„ Seminum Cannabis	846	Enesol (injected), 1 gr. in 30 m.	189
„ Sesami, 2 to 3 oz. <i>p.d.</i>	876	Eno's Fruit Salt	628
			Entamoeba Cysts, Search for... ..	529 &	542
			„ Buccalis	927
			„ Coli ...	541 et seq.	
			„ histolytica 526 et seq. & 541 et seq.		
			„ Nana	542
			Entericin	871
			Enteric Fever. See Typhoid.		
			Enterococcus	574

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Enzyme Action...	548, 637 & 76		Essence of Beef	582
Enzytol, 3 to 20 Cc. dil.	...	5	Essence of Ginger, 895; Vanilla	...	893
Eosin Stains (various) .	399, 614		„ „ Rennet	661
Eosote, 5-10 m.	387	Essentia Yerba Buena (Ph.	...	
Eparseno	202	Notes)=Mentha Sativa.	...	
Ephedrine ...	855, 165, 224		Essential Oils as Antiseptics	600, 126	
„ Hydrochlor., $\frac{1}{2}$ to 2 gr.	855		„ „ in Cholera ...	1046	
„ Sulphas, $\frac{1}{2}$ to 2 gr.	...	855	Essential Oils, Terpeneless	123, 125	
Ephetonin ...	856, 165		Essogen	102
Epidemic encephalitis	545	Ethanesal	102
Epilepsy, non-specif. protein,	...		Ethanol. U.S. Syn. of Ethyl	...	
671; Luminal 822 & Ther.	...		Alcohol.	...	
Ind.	1059	Ether	101
Epinephrin ...	976, 170		„ Chloric	290
Epinine ...	982		„ Convulsions	102
Epsom Salts (Mag. Sulph.)	...	546	„ Green	284
Equisetum Arvense	856	„ Ozonic	495
Erasmus Wilson's Lotion	...	149	„ Perles, 3 m. in each	109
Erdmann's Test	204	„ Petroleum	660
Erepsin	76	„ Regulations N. Ireland..	28	
Ergamine	407	„ Soap, et c. Merc. Iodide...	762	
Ergoapiol	169	„ with Atropine	105
Ergosterol Estimation...	...	105	„ with Olive Oil	107
„ Irradiated ...	597, 104		„ with Oxygen and Alcohol	...	104
Ergot, 15 to 60 gr. ...	403 & 77		„ with Oxygen and Gas	104
Ergot Aseptic	404	Ether with Paraff. Liq. Oral use	...	108
„ of Maize...	868	„ with Saline	105
„ Physiol., Standardised	...	77	<i>v. also Aether.</i>	...	
Ergotamine ...	403, 408		Ethidol, 3 grains	622
„ Tartrate	406	Ethocaine Berate, $\frac{1}{2}$ to 1 $\frac{1}{2}$ grains	...	349
Ergotin 2 to 8 gr.	405	Ethocaine HCl, 1/5 to 1 gr.	346
Ergotinine Cristallisée, 1/200 to	...		Ethoxy Diamino Acridine Lact.	...	307
1/64 gr. ...	406, 224		Ethyl Acetate ...	110, 442	
„ Cit., 1/150 to 1/30 gr.	406		„ Alcohol ...	113, 22	
Ergotoxine, 1/100-1/50 gr.	403, 406		„ Amino-benzoate	350
„ Ethane sulphonate,	...		„ Bromide (Caps. 5 m.)	836
$\frac{1}{100}$ to $\frac{1}{50}$ gr. hyp. ...	406		„ Butyrate ...	840, 28	
Ergoval, 10 to 30 m. or 60 m....	404		„ Carbamate, 10 to 60 gr.	824	
Eriodictyon	394	„ Chloridum (Bulbs, tubes	...	
Erica Heather, Ericolin Separation	...		and bottles, 111) ...	110	
of T.B. <i>v.</i> Edn. XVIII.,	575		„ „ Dangers	111
Erigeron Can.	856	„ „ Inhaler.	111
Ernutin, 30 to 60 m.	406	„ „ Medictd. Solns.	111
Erodium	856	„ Esters Chaulmoogra, 1	...	
Erucae Semina (Sinapis) ...	763		Cc. intram. 609;	...	
Eryngium	856	Iodized	610
Erysipelas Dressing, 830; Serum	928		„ Gas	151
Erysimum	856	„ Group effect of	254
Erythrol Nitrate, $\frac{1}{2}$ to 1gr. incr.	408, 224		„ Hydrocarbate	612
Erythrophlœinæ Sulph., 1/40 to	...		„ Hydro-Cuprcine, Base 3	...	
1/24 gr.	409	to 4 gr., 387; HCl., 3	...	
Erythrosins	399	to 4 gr.	388
Erythrotetranitral, $\frac{1}{2}$ to 1 gr. incr.	408		„ Iodide and Sterules, 5 m.	112, 271	
Erythroxyton Coca, 30 to 120	...		„ „ c. Chlorof. Sterules...	112	
gr.	331	„ -iodo-ricinoleate, 3 grains	622	
Esanofele	740	„ Lead	659
Esbach's Picric Solution ...	363		„ Morphine (Base) ...	566, 139	
Eserina, $\frac{1}{100}$ to $\frac{1}{50}$ gr. ...	693		„ HCl., $\frac{1}{2}$ to $\frac{1}{2}$ gr.	565, 224	
Eserinæ Salicyl., 693; Sulph.,	...		„ Narceine and HCl. ...	872	
1/60 to 1/20 gr. ...	693		„ Nitrite Sol., 15 to 60 m.	110	
Esprit var, vide Spiritus	—	„ Oxide	101
„ Ammonia. Anisat ...	860		„ Petrol	151
Esparto	856	„ Salicyl	73
Espundia	552	„ Theobromine	163

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Ethyl para Meth. Phenyl Cin- choninate		319	Ext. Allii, 4 to 10 gr. ...		837
Ethylene		291	„ Alni Glutinosæ Liq., 10 to 30 m.		838
„ Promide, 1 to 2 m. ...		836	„ Aloes, 1 to 4 gr. ...	137, 311	
„ Dichlor... ..		292	„ Anthemidis, 2 to 8 gr. ...		840
„ Glycol		431	„ Apocyni Liq., 15 m. ...		170
Eucaine Borate		349	„ Belæ Liq., 1 to 2 dr. ...		844
„ HCl. 1/10- $\frac{1}{2}$ gr. ...		344	„ Bellad. Sicc., $\frac{1}{4}$ -1 gr. 224 & 47		
„ Lact. $\frac{1}{2}$ to $\frac{1}{2}$ gr. ...		344, 224	„ Bellad., Fol., av. $\frac{1}{4}$ gr. 224, 225		
„ c. Adrenalin		344	„ „ Liq., $\frac{1}{2}$ -1 m. ...		224
Eucalypti Folia, 5 gr. ...		613	„ „ Viride, $\frac{1}{4}$ to 1 gr. 225 & 43		
„ Gummi, 2-5 gr. ...		856	„ Bone Marrow, 1-2 dr. ...		958
Eucalyptol, 1 to 4 m. 614, 129, 224			„ Brain, 5 to 10 m. ...		959
„ Chlorinated		53	„ Buchu Liq. 30 m. ...		845
„ Phosphate, 1 to 5 gr. 615, 129			„ Bynes (and Liq.), 1 to 4 dr.		548, 549
Eucodal, Eukodal	xxxvii		„ Caeti Grandi. Liq., 1 to 10 m.		849
Eucerin		815	„ Calumbæ, '85, 2-10 gr. ...		—
Euchlorine Gargle		773	„ Cannabîs Ind., $\frac{1}{4}$ -1 gr. 266, 54		
Eucodeine, $\frac{2}{3}$ gr.		357	„ „ Liq., $\frac{1}{2}$ m.		267
Euflavine (Tablets, per os $\frac{1}{2}$ grain 306)		305	„ Capsici Liq., 1 m. ...		272
Eugallol		64	„ Carnis		581
Eugenol ... 410, 847, 857, 878			„ Cascaræ Sag., 2 to 8 gr. ...		277
Eumenthol Jujubes		615	„ Cascaræ Sagradæ Liq., 30 to 60 m.		277
Eumydrine		217	„ Cascara Aromat. Liq., 30 to 60 m.		278
Eunatrol		761	„ Catha Solid., 2 $\frac{1}{2}$ to 10 gr. 847		
Euonymi Cortex		410	„ „ Liq., 1 to 5 m. ...		847
Euon/min, 1 to 2 gr. ...		410	„ Caulophylli Liq., 8 m. ...		848
Eupad		48	„ Cerebri Liq., 5-10 m. ...		959
Eupatorium		857	„ Cerevis Ferment. 3 gr. 280, 98,		
Euphorbia Peplus Pil. ...		857	„ „ 506		
Eupnine, 1 dr.		251	„ Cerii Liq., 1 to 10 m. ...		849
Euquinine, 3 to 15 gr. ...		741	„ Chanvre		266
Eureka Weed Killer		35	„ Chekan, Liq., $\frac{1}{2}$ -3 dr. ...		850
Euresol		752, 226	„ Chelid. Liq., 10 to 30 m. ...		850
Eurobin		295, 226	„ Chenopodii Liq., $\frac{1}{2}$ to 1 dr. 850		
Eusol		46, 272	„ Chinæ, 1 to 4 gr. ...		297
„ Assay		8	„ Chirataë Liq., 15 m. ...		851
„ Bactericidal Power ...		8	„ Cigue, $\frac{2}{3}$ gr.		382
„ Intravenous Use		47	„ Cimicifugæ Liq., 5-30 m. 851		
„ Uses, 46; Cordova's Modif. 48			„ Cinchonæ Liq., 5-15 m. 297 & 60		
Eustachian Self-Inflator ...		289	„ Cocæ, 2 to 15 gr. ...		332
Eustenine, 8 to 15 gr. ...		806	„ „ Liq., $\frac{1}{2}$ -1 dr. ...		332
Evans' Antiseptic Throat Pas- tilles		628	„ Colchici. $\frac{1}{4}$ to 1 gr. ...		358, 69
Euxenite		324	„ Collinson, Liq., 15 to 30 m. 852		
Evatmine.		978	„ Colocynth., av. $\frac{1}{4}$ gr. ...		380
Evonymine		410	„ Colocynth. Comp., 2 to 8 gr.		380
Ewald's Breakfast		415	„ Condurango Liq., 10 to 60 m.		852
Ewin's Test		170	„ Conii, max. $\frac{4}{5}$ gr. FR. Cx. 382		
Exalgine, $\frac{1}{2}$ to 2 gr. ...		3, 226	„ „ Liq., 5 to 15 m. ...		382
Exibard's Pdr.		717	„ Convallariæ, 2-8 gr. ...		852
Excise Duty		114	„ Coorchi Liq.		862
Exogonium		864	„ Corn Silk, Liq. 1 dr. ...		868
Explosives		13	„ Coronilla, 1 $\frac{1}{2}$ gr. ...		852
EXTRACTA :			„ Coto Liq., 2 to 6 m. ...		382
(vide also Fluidextr.)			„ Cyperi Rot. Liq., 15 to 60 m.		854
„ Acocantheræ Liq. max. 4 m. (?)		835	„ Damianæ, 2 to 10 gr.; Liq., $\frac{1}{2}$ to 1 dr. ...		854
„ Aeoniti Rad. Ale., max. $\frac{1}{2}$ gr.		98, 20			
„ Agarici, $\frac{1}{2}$ to 2 gr. ...		836			
„ Agropyri Liq., 1 to 2 dr. .		837			
„ Aletridis, Liq., 5 to 15 m. 837					

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Ext. Digitalis, FR. CX. (U.S.,			Ext. Ipecac. ...		524
av., $\frac{1}{2}$ gr.) ...		395			
„ d'Orges ...		548	„ Ipecac. { Expectorant		524, 89
„ Duodenal Liq., 5 to 20 m.		960	„ Liq. { $\frac{1}{2}$ to 2 m.		
„ Ergotæ, 2 to 8 gr. ...		405	„ Liq. { Emetic, 15		
„ „ Liq., 10 - 30 m. ...		404	„ „ to 20 m. ('98)		
„ „ Phys. Stand. ...		404	„ Iridis 1 to 3 gr. ...		864
„ Erigeron Liq., 30-60 m. .		856	„ Jaborandi, 2 to 10 gr.,		
„ Erodii Liq., 15 m. ...		856	(B.P. '85) ...		—
„ Erythroxyl Liq., $\frac{1}{2}$ -1 dr..		332	„ „ Liq., 5 to 15 m. ...		696
„ Eucalypti Gum. Liq., 30			„ Jalapæ, 2 to 8 gr..		864
to 60 m. ...		856	„ Kavæ, 5 to 10 gr..		865
„ Euonymi, 1 to 2 gr. ...		410	„ „ Liq., 30 to 60 m. ...		865
„ „ Liq., 10 to 60 m. ...		410	„ Kolæ Liq., 10-20 m. ...		252
„ Eupatorii Liq., 30 m. ...		857	„ Krameriaæ, 5-15 gr.; Liq.		
„ Euphorbiæ Pepli, $7\frac{1}{2}$ to			15 m. ...		—
30 gr. ...		857	„ Kurchi Liq. ...		862
„ Euphorbiæ Pil., $\frac{1}{2}$ to $1\frac{1}{2}$ gr.		857	„ Lactucæ, 85, 5-15 gr. ...		—
„ Eye, 2 dr. .		961	„ Lappæ Liq., 30 m. ...		866
„ Fæcis ...		280	„ Lasiosiphon Liq., 2 to 5 m.		867
„ Fæxin, 3 gr. ...		280	„ Leptandræ, av. 4 gr. ...		867
„ Fellis Bov. ...		411	„ Leeches ...		961
„ Ferri Pomatum ...		416	„ Liver Dessic. & Liq. ...		962
„ Filicis Liq., 45-90 m. 422, 30			„ Lupuli, 2 to 6 gr. ...		868
„ Frangulæ Liq., 1-4 dr. ...		858	„ Lupuli, Liq., 5 to 15 m....		868
„ Fuci Vesic., 3 to 10 gr. 858			„ Maidis Stig. Liq., 1 dr. ...		868
„ „ Liq., 1 to 2 dr. 858			„ „ Ustil. Liq., $\frac{1}{2}$ to 2 dr.		868
„ Galega, 5 to 10 gr. ...		858	„ Malti (& Liq.), 1 to 4 dr.		548, 549
„ Galii, 5 to 20 gr. ...		858			
„ Gastricum, 1 to 2 dr. ...		663	„ „ Ferratum ...		550
„ Gelsem Liq., $\frac{1}{2}$ m. ...		426	„ „ c. Cascara ...		550
„ Gelsem. Pulv., $\frac{1}{2}$ -2 gr. ...		426	„ „ c. Hæmoglobin .		550
„ Gentianæ, 2 to 8 gr. ...		859	„ „ c. Hypophos. ...		550
„ Geranii Mac. Liq., 15 m. 859			„ „ c. „ et Ol. Morr-		550
„ Glaucii Liq., 1 dr. ...		859	„ huæ ...		
„ Glycyrrhizæ, 5-60 gr. ...		860	„ „ c. Glyceroph. ...		
„ „ Liq., 30-60 m. ...		860	„ „ c. Iodinol (1 oz.		40
„ Gokhru Liq., 20-60 m. ...		860	„ „ dose) ...		
„ Gossypii, 1 to 4 gr. ...		443	„ „ c. Oleo Morrhuæ		550
„ „ Liq., $\frac{1}{2}$ to 1 dr. ...		443	„ „ c. Pancreatin ...		550
„ „ Sem., 1 dr. ...		443	„ „ Sicc., 1 to 2 dr. ...		550
„ Granati Liq., 30 m. ...		660	„ „ c. Syr. Ferri Phosph.,		
„ Grindeliæ, 2 to 3 gr. ...		444	1 to 4 dr. ...		550
„ „ Liq., 10 to 20 m. ...		444	„ Paraff. ...		549, 551
„ „ Co., 1 dr. ...		444	„ Manacæ Liq., 10-30 m. ...		868
„ Guaranæ Liq., $\frac{1}{2}$ dr. ...		861	„ Meat ...		581
„ Hæmatoxyli Liq. (& Solid,			„ Menyanthis Liq., $\frac{1}{2}$ oz. ...		870
av. 15 gr.), $\frac{1}{2}$ to 2 dr. ...		861	„ Monsoniæ Liq., 10 to 30 m.		871
„ Hæmostatic ...		405	„ Muira Puama ...		871
„ Hamamelidis Dest., $\frac{1}{2}$ to			„ Myrtilli Liq., 2 ozs. p.d....		872
3 dr. ...		448	„ Nucis Vom., $\frac{1}{2}$ to 1 gr. ...		599
„ „ Liq., 5-15 m. ...		448	„ „ Liq., 1 to 3 m. 599 & 123		
„ Helenii ...		864	„ „ Opil Siccum (20% Morph.),		
„ Hippocast Liq. ...		835	$\frac{1}{2}$ to 1 gr. ...		629
„ Holarrhenæ Liq....		862	„ „ Liq. (0.75% Morph.),		
„ Humuli, 2 to 6 gr. ...		868	5 to 30 m. ...		629
„ Hydrastis, 2 to 5 gr. ...		492	„ Papaveris, 85, 2 to 5 gr. —		
„ „ Liq., 5-15 m. ...		492	„ Parathyroid Liq. .		993
„ Hyoscy., 2 to 8 gr. ...		501	„ Pareiræ Liq., 30 to 120 m.		876
„ „ Viride, 2-8 gr. ...		501	„ Physostigmat., $\frac{1}{2}$ to 1 gr.		693
„ Hypophysis, $\frac{1}{2}$ to 1 Cc....		968	„ Pichi Liq., 10 to 60 m. ...		877
„ Hysterionicaæ Liq., 5 to 15			„ Picorrhizæ Liq., 15 to 60 m.		877
m. ...		863	„ Pini Canad. Liq., 10 to		
„ Infundibular, $\frac{1}{2}$ to 1 Cc....		968	60 m. ...		878
„ Inulæ Liq., 10-60 m. ...		864	„ „ Sylvestris .		701

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Ext. Piscidiæ, 2 to 5 gr.; Liq.			Ext. Valerianæ (Liq., 30 m.),		
20 to 120 m. ...	878		1 to 5 gr. ...	822	
„ Pituitary Gland <i>Infund.</i> $\frac{1}{2}$			„ Viburni Prunif., 2 to 10		
to 1 Cc. ...	968		gr., <i>Liq.</i> , 60 to 120 m..	894	
„ „ Entire Gland, $\frac{1}{2}$ to			„ Vincæ Majoris Liq., 1 to		
1 Cc. ...	968		2 dr. ...	894	
„ „ Ant. lobe, 1 Cc. ...	968		„ Violæ Liq., 1 dr. ...	894	
„ Pulsatilla Liq., 2 to 5 m. .	879		„ Water Germander Liq.,		
„ Quassiæ, 3 to 5 gr. ...	880		$\frac{1}{2}$ to 1 dr. ...	890	
„ Quebracho Liq., 5 to 10m. .	881		„ Yeast ...	280, 500	
„ Quillaia Liq. ...	881		„ Yerbæ Santæ, 10 to 40 m.	894	
„ Quinquina Rouge Liq. .	297		Eye Bottles, 214; Extract, 961;		
„ Red Bone Marrow, 1 to 2 dr.	958		Lotion Cocaine (Factory),		
„ Retinæ, 2 dr. ...	961		335; & Lotion Iso-tonic,		
„ Rhamni Frang., 15 to 60			338; Operation Sets, 437;		
gr.; Liq., 1 to 4 dr. ...	858		Pads, 436; Rods, 214; Wash,		
„ „ Pursh., av. 4 gr. ...	277		Mackenzie ...	468	
„ „ Fluid	277		Factory Act Eye Drops ...	338	
„ <i>Rhei</i> , 2 to 8 gr. ...	881		Fæces, Exam. of. ...	12, 411	
„ Rhus Aromat. Liq., 10 to			Fæx Medicinalis, $\frac{1}{2}$ to 1 oz. ...	279	
30 m. ...	882		Fæxin, 1 dr. ...	280	
„ Rice Polishings ...	506		Fæxin, Extr. Pills, 3 gr. ...	280	
„ Rubi Chamæmori Liq.,			„ Extr. Tablets, 3 gr. ...	280	
$\frac{1}{2}$ to 1 dr. ...	883		Faivre's Cachets ...	252	
„ Salicis Nig. Liq., $\frac{1}{2}$ to 1 dr.	883		Faraday's Electro Chem. Equiv.	286	
„ „ Solid, 1 to 5 gr. ...	883		Farrant's Medium ...	616	
„ Sanguinariæ, Liq., $1\frac{1}{2}$ m.	884		Fats, 601; as foods, 94, 96;		
„ Sansivieræ, 10-20 gr.;			Iodine, Nos. 86, Melting Pts.,		
Liq., 2 to 4 dr. .	884		248; Sapon. Figs. ...	159	
„ Sarsæ Liq., 2 to 4 dr. ...	884		Fatty Acids unsaturated ...	616	
„ Saw Palmetto, 3-5 gr.;			Favus ...	1093, 569	
Liq. $\frac{1}{2}$ to 2 dr....	885		Feathers... ..	665, 666	
„ Scillæ ...	885		Fedrin, $\frac{1}{2}$ to 2 gr. ...	855	
„ Scutellaria Liq., 5 to 15 m.	885		<i>Fehling's Solution</i> and Modifs. .	373	
„ Secretin, 5 to 20 m. ...	960		„ „ Sterules ...	374	
„ Senecio, Liq., 20-60 m....	886		Felamine	454, 783	
„ Senegæ Liq. ...	168		<i>Fel Bovinum Purif.</i> , 5-15 gr....	411	
„ Sennæ Leg. Liq., 1-2 dr..	886		„ Exsicc., 5 to 10gr. 411		
„ Serpentar Liq., 5 to 15 m.	886		Fellows' Syrup of Hypophos-		
„ Solani Tub. Liq., 1 to 4			phites, medium adult, 1 dr.		
dr. ...	887		692 & 629		
„ Sorbi Liq., 10 to 30 m. ...	887		Felt, 436; Femergin Tablets		
„ Spinal Cord, 5-20 m. ...	959		(Sandoz), 406; <i>Fennel</i> , ...	857	
„ Stramonii, $\frac{1}{2}$ to 1 gr. ...	788		Ferascol ...	883	
„ Strawberry Eth. .	858		Fermentactyl ...	57	
„ <i>Strophanthi</i> , $\frac{1}{4}$ -1 gr. ...	790		Fermentation Test ...	378	
„ Strychni, $\frac{1}{4}$ to 1 gr. ...	599		Ferments, <i>see</i> Enzymes ...		
„ Sumbul Liq. U.S., av. 30			Ferri Alginas, 2 to 15 gr. ...	837	
m. ...	889		„ Arsenas, 1/16 to $\frac{1}{4}$ gr. ...	184	
„ Supra-renal Liq. 10 to			„ Cacodylas, $\frac{3}{4}$ to 5 gr. ...	186	
15 m. ...	976		„ Carb. Sacch., 10-30 gr. ...	411	
„ „ Sicc., $\frac{1}{2}$ to 3 gr. ...	975		„ Conc. ...	412	
„ Symphiti, 5 to 10 gr. ...	889		„ Chlorid.. U.S. = Ferri		
„ „ Liq., 2 to 4 dr. ...	889		Perchlor. ...	413	
„ Tanaceti Liq., 15-30 m....	890		„ Citras, av. 4 gr. ...	412	
„ <i>Taraxaci</i> , 5 to 15 gr. ...	890		„ et Ammon. Cit., 5 to 10 gr. 412, 79		
„ „ Liq., $\frac{1}{2}$ to 2 dr. ...	890		„ „ Virid., 5 to 10 gr. 412, 79		
„ Tebalaco, $\frac{1}{2}$ to 1 gr. ...	629		„ „ Sulph., 3 to 10 gr....	421	
„ Thymi Liq., 5 to 30 m....	892		„ „ Tart., U.S., 4 gr. ...	421	
„ Thymus Gland, $\frac{1}{2}$ -2 dr....	983		„ et Mag. Sulph., 2 to 10 gr. 421		
„ Thyroid = Thyroid Sicc.,			„ „ Mang. Citras, 3 to 15 gr. 421		
988; Liq. Thyroid ...			„ „ Potass. Tart., 5 to 10 gr. 421		
987 & 171			„ „ Quin. Citras, 5-10 gr. 726		
„ Tritici Liq., 1-2 dr. ...	837		„ „ „ Eff., 3 grs. ...	720	
„ Uvæ Ursi Liq., av. 30 m. .	841				

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Ferri Quin. et Strych. Cit.			Filaria Dracunculus ...		550
3 to 6 gr. ...		726	Fildes Medium ...		551
" " Strych. Cit., 2 gr. ...		792	Filicin ...		423
Fluoridum, $\frac{1}{20}$ to $\frac{1}{2}$ gr. ...		833	Filmaron .		423
Formas, $1\frac{1}{2}$ to 3 gr. ...		35	Filmaronöl ...		423, 424
Glyceroph., 1 to 5 gr. ...		37	<i>Filix Mas</i> ...		422, 80
Hydrox. c. Mag. Ox. ...		180	Filter passing Influenza Virus		923
Hypophosph., 1-5 gr. ...		691	Finsen Reyn Lamp ...		314
Iodidum, 1 to 5 gr. ...		416	Fireproofing ...		776
Iodid. Sacch., 2-15 gr. .		417	Fir, Douglas ...		148
Lactas, 1 to 5 gr. ...		56	" Oregon ...		148
Lactoph. et Calci (Syrup)		56	" Scotch ...		699
Nucleinas, 15 gr. ...		415	Fir Wool, Oil, and Extract ...		701
Oleas, 5 to 15 gr. ...		604	Fire Extinguisher ...		776
Oxalas, 1 to 5 gr. ...		417	Fischer's Modifd. Ringer Soln.		767
Oxydat. Sacch., 10 to 40 gr. ...		415	Flag ...		864
Oxypersulphas (Monsel's)		421	Flagella Stains ...		605
Peptonat, 416; Liq., 1-4 dr.		415	Flagellate dysentery ...		543
Perchlor. (wool, 413), 2-8 gr. ...		413	Flaginac .		437
Persulph. ...		421	Flame Tree ...		864
<i>Phosphas Saccharatus</i> , 5 to 10 gr. ...		418	Flavoring Agents ...		433
" Solubilis, 4 gr. ...		418	Flavine ...		300, 272
Pyrophosph., U.S., 4 gr.		418	Flax Seed, 867; Tow ...		437
Salicylas, 3 to 10 gr. ...		67	Fleabane .		856
Sesquichlor. ...		413	Fleming's Liq. Chrom. Acct.-Osmic .		834
Subsulph. ...		421	Fleming's Neutral Red Medium		927
Succinas ...		835	" Syph. Test <i>see</i> XVIIth Edn.		
Sulphanilas ...		309	" Tinct. Aconite, 1 to 5 m.		99
<i>Sulphas</i> (Granulat., U.S.), 1 to 5 gr. ...		420	Fletcher's Artif. Dentine ...		830
" <i>Ersicc.</i> , $\frac{1}{2}$ to 3 gr. ...		420	Flexner's Serum ...		912
Tersulph. ...		421	Flies to ward off, <i>vide</i> Therap. Index, Bites and Stings.		
Valerianas, 3 to 15 gr. ...		825	FLOUR Acid Phosphates in, <i>et seq.</i>		116
Ferrier's Snuff ...		236	" Analysis Expts. ...		117
Ferrinol, 15 gr. .		415	" Baking Powders... ..		114
Ferrivine .		309	" Benzoyl Peroxide in ...		120
Ferro-Alumen, 3 to 10 gr. ...		421	" Bleaching... ..		112
Ferrocarnis, 1 dr. ...		582	" Detection of ...		117
Ferro Mang. Phosph., 3 to 10 gr.		552	" Blends of... ..		120
Ferropyrin, 3 to 8 gr. .		329	" Calc. Sulphate in ...		114
Ferro-sajodin Tabs., $7\frac{1}{2}$ gr. ...		522	" Chlorine in ...		116, 120
Ferro-Silicon ...		80, 142	" Coloring Matter of ...		114
Ferro-Titanium... ..		58	" Depart. Ccm. '27 Rept....		120
Ferruginous Ampoules ...		40	" Germ in ...		108 <i>et seq.</i>
<i>Ferrum</i> ...		411 & 73	" "Graham" ...		107
<i>Redactum</i> , 1 to 5 gr. ...		411	" Improvers ...		115
<i>Tartaratum</i> , 5 to 10 gr. .		421	" Iodine in ...		109
Ferula Fœtida .		842	" "Mill Stone" ...		107
Fève de St. Ignace ...		599	" Mineral and other constituents of ...		109
Fever <i>see</i> Diseases in question, also Table p. 996.			" Moisture in ...		118
Fever as a Salutory reaction...		299	" Offals removed ...		109
Fever Powders ...		738	" Nitrites in ...		113 <i>et seq.</i>
Fevillea ...		857	" National Mark ...		112
Fibrin ...		76	" Persulphates in ...		116
Fibro-coumaria Sterules, 25 m.		27	" Phosphorus in ...		110
Fibrolysan ...		764	" Potato Starch in... ..		117
Fibrolysin, 1 to 2 Cc. ...		764	" Self Raising ...		114
Ficus Carica ...		857	" Standardisation, etc. ...		107
Field Day ...		159	" Stone Ground ...		107
Fig ...		857	" "Stone Milled" ...		107
Filaria ...		Therap. Ind. & 545	" Survey of Flour & Bread		119
			" Vitamin B. of White ...		111
			" Wholemeal ...		107

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Flour, Wholemeal Roughage of		149	Fluorine		272
Fluid Magnesia, 1-2 ozs. . .		545	Fly Deterrents & Destruction		1037
Fluidextr. Aconiti, av. $\frac{1}{2}$ m. . .		98	Fly Papers, Arsenic		35
„ Apocyni, 15 m.		170	„ „ Sticky		894
„ Bellad., Rad., $\frac{3}{4}$ m.		225	Fly, Spanish or Blistering . . .		267
„ Buchu, 30 m.		845	<i>Faniculo Eructus</i> , 857; <i>Fœnu-</i>		
„ Calami, 15 m.		—	greek		857
„ Cannab. Ind., 1 $\frac{1}{2}$ m.		267	Folin and Wu Method		407
„ Capsici, 1 m.		272	Folin's Blood tube		407
„ Caseara		277	Fontana's Stains		573
„ „ Aromat., 30 m.		278	Food and Drugs Act, 1928 . . .		491
„ Chiratae, 15 m.		851	Food Colours	2, 495	
„ Cimicif., 15 m.		851	Foods, 581 <i>et seq.</i> 94; Calorie		
„ Cinchonæ, 15 m.		297	Values of various, 97; Dia-		
„ Coeæ, 30 m.		332	betie, 591; Infants', A.B.C.		586
„ Colehici Sem., 3 m.		358	Foods, Doctoring of		495
„ Conii, 3 m U.S.		—	„ Iodine in		429
„ 0.45% Conine		—	„ Poisoning	502, 509	
„ Convallar., 8 m.		852	„ Preservatives 2, 13, 492, 493		
„ Ergotæ, 30 m.		404	„ Vitamins in		93
„ Eriodietyi, 10-40 m.		894	Food Iron		73
„ Eupatorii, 30 m.		857	Food Factors, Accessory	592, 93	
„ Frangulæ, 1-4 dr.		858	Food Poisoning	1039	
„ Geranii, 15 m.		859	„ „ Metal contamination		1040
„ Granati, 30 m.		660	Fool's Parsley		836
„ Guaranæ, 30 m.		860	Foot and Mouth Disease . . .		716
„ Hamamelid. Fol., 30m.		448	Foot Powder		142
„ Hyosey., 3 m.		501	Foreign-made goods		623
„ { Ipeecæ., Emetic, 15 }		524	Forest Yaws		552
„ { m. Expt., 1m. }		—	Formagules (Benzol, 310; Olive		
„ Lappæ, 30 m.		866	Oil, 619; Santalol, 622)		698
„ Phyto. { Emetic, 15m. }		877	„ Naphthalene Tetrachlor		573
„ lacc. { Alterat., 1 $\frac{1}{2}$ m }		—	Formaldehyde, 126, 22, 272; . . .		
„ Pilocarpi, 30 m.		696	in Food, 494; Glycerin, 128; . . .		
„ Pruni Virginianæ		—	Formaldehyde Tablets, In-		
„ (Glycero - hydro -		—	ternal	132, 30	
„ alcoholic), 30 m.		—	Formaldehyde, Production by		
„ Quassia		880	Bacteria		30
„ Quillaia, 3 m.		881	Formaldehydum Polymerisatum		
„ Rhei, 15 m.		881	= Paraform		131
„ Rosæ, 30 m.		882	Formalin, Formol, 126, 226; . . .		
„ Rubi, $\frac{1}{2}$ to 1 dr.		883	Chlorof. Sols., 129; Dis-		
„ Sanguinariæ, 1 $\frac{1}{2}$ m.		884	infecting Tablets, 131; Gargle		
„ Sarsaparillæ, 2 to 4 dr.		884	128; Inhalation, 129; as Meat,		
„ Scilla, 1 in 1, 1 $\frac{1}{2}$ m.		885	etc., Preservative	29, 30, 616	
„ Scutellariæ, 5 to 15 m.		885	Room Fumigation		131
„ Senegæ, 15 m.		886	Tabs Internal assay		30
„ Spigeliæ, 1 dr.		888	Formalinsapa		130
„ Staphisagriæ, 1 m.		888	Formalised Gelatin		425
„ Stillingiæ, 30 m.		888	„ „ (Capsules		698
„ Stramonii, 1 m. (0.25		—	Formamide		129
„ per cent. alk.)		—	Formamin		450
„ Sumbul, 30 m.		889	„ Ethyl Iodide		510
„ Tritici, 1 to 2 dr.		837	Formamint Tablets		132
„ Uvæ Ursi, 30 m.		841	Formanganate Disinfectior. . . .		272
„ Valerianæ, 30 m.		825	Formanilid, 2 to 4 gr.		129
„ Viburni Prunif. 1 to 2		—	Formic Preservative		34
„ dr.		894	Formidin Gze. and Tape		510
„ Xanthoxyli, 30 m.		894	Formin, 5 to 15 gr.		450
„ Yerba Santa, 15 m.		894	Formosyl, 129; Dental Dress-		
„ Zingib. 8 m.		895	ings, 130; Mouth Wash, 130; . . .		
Fluid-glycerates		433	Tooth Paste, &c., 130; . . .		
Flumerin		478, 212	Gargle, 130; Glyc. Soap, 762; . . .		
Fluorescein, 678, 226; in Cancer		531	Pastils, 130; Pessaries		130
„ Mercury Comps. 478, 479		—	Formosyls, Perfumed		600

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE
Formyl Terchloride, 1-5 m. ...		284
Fotus Acid Borici, 6 dr. to 1 pint		
„ Belladonnæ, 1 to 2 dr.		
„ of Tinct. to 1 pint ...		
„ Opii, ½ to 2 dr., to 1 pint		
„ Papaveris, 2 ozs. to 1½		
„ pints, 15 minutes;		
„ foment at 120° F. ...		
Fouchet Test ...		612
Four Gland 'Tablets' ...		989
Fourneau '309' ...		316
Fournier's Syringe ...		455
Fowler's Solution, 2 to 8 m....		180
Fragaria ...		858
Fraisse's Ferrug. and Serum		
„ Ampoules ...		40
Frambœsia, 612; Frangula		858
Frankincense ...		699
Fraser's Root ...		845
Fraser's Tinct. Strophanth. ...		791
Fraxinus ornus... ..		868
Fredericia's CO ₂ tensimeter, see		
„ Edn. XVIII., 376.		
Freeman's Chlorodyne .		629
Freezing Mixtures ...		249
French Chalk, 144; Glossary..		642
„ Polish ...		122
Friar's Balsam, ½ to 1 dr. ...		6, 3
Friedländer's Pneumo.bacillus		567
Frigidaire Cabinet ...		485
Fröhde's Reagent ...		73, 204
Fröhlich Syndrome ...		990
Frost Bite ...		1062
Frost's Solution ...		616
Fructolax, 2 to 3 dr. ...		657
Fructose... ..		757
Fruit Preservatives ...		493, 500
Fuch sine, Basic and Acid, or		
„ S, 532; (Carbol Solu-		
„ tion) ...		226, 532
„ ½ to 4 gr. ...		320
„ Ointment ...		320
„ Aniline Green ...		553
Fuch sine Sulphurous Acid Test		24
Fucus Vesiculosus ...		858
Fullers' Earth ...		143, 374
Fuller's Inhalant ...		446
Fulmar Oil ...		143
Fumigators ...		128, 272
Fumus Potassii Nitratis ...		717
Fungi, poisoning by (see Poisons		
„ and Antidotes).		
Fungi as Urine Tests ...		379
Fungus igniarius, P. Austr. ...		838
„ Laricis ...		836
Fur Dyes ...		308, 1051
Fur, Antimony in ...		33
„ Dermatitis ...		308, 1051, 33
Furfural ...		132
Fusel Oil ...		119
Gaertner Group ...		509, 550
Galactose ...		758
„ or B. typhosus, v. Edn.		
XVII., p. 551.		

NAME.	DOSE.	PAGE
Galangal, 858; Galbanum, 5 to		
„ 15 gr. ...		858
Galega, 858; Gale, Sweet ...		844
Galegin ...		651
Galium Aparine, 858; Galla, 7½		
„ gr. av. ...		858
Gall Bladder Visualisation ...		680
„ „ „ Sod. Brom.		771
„ „ „ Treatment		681, 1062
Galvanometer ...		283
Gambir, 848; Gamboge, ½ to 2 gr.		845
Gamgee (Gauze and Wool)		
„ Tissue ...		436
Ganja ...		266
Garcinia Hanburii ...		845
Gardenal, 1½ to 5 gr. ...		822
Garfield's Tea ...		717
Gargar. Acidi Benzoici .		6
„ Acid Carbolici ...		16
„ Acidi Tannici .		95
„ Aeruginis ...		389
„ Aluminis ...		429
„ Carbolica ...		16
„ Chlori ...		773
„ Formaldehydi ...		128
„ Formosyl ...		130
„ Hyd. Co. ...		475
„ „ Perchlor ...		469
„ Hydrog. Perox. ...		495
„ Potass. Chlor. ...		711
„ „ Permang. ...		553
„ Resorcini ...		752
Garlic, ½ to 2 dr. ...		837
Garrod's Lozenges ...		798
Gas, Dental ...		146
„ Gangrene, 546; Serum		
„ used in Peritonitis and		
„ Toxæmia, Therap Ind.		
„ Mantles ...		807
„ Oxygen and Ether ...		104
„ Poisoning ...		1101, 500
Vide also Respirator Soln. p. 94		
Gasoline ...		659 & 144
Gastric Contents Examn. ...		415
„ Ulcer ...		1095
Gaubius' Table of Dosage ...		1108
Gauducheau's Stain ...		558
Gautiers Pills ...		629
Gauze-covered Moss ...		786
Gauze, Bismuth Subgallas		237
„ Bromphenobis ...		20
„ Carbolised ...		16
„ Cyanide... ..		462
„ Chinosol ...		317
„ Iodoform ...		436, 508
„ Mercuriome ...		480
„ Picric ...		63, 436, 438
Gauzes and Gauze Tissues		436, 438
„ Tampons ...		436
Gazoline ...		660
Gee's Cough Linctus, 1 dr. ...		629
Gelanthum ...		813
Gelatin Glycerin ...		430
„ Injections ...		1, 424
„ Nutrient (Bact.) .		617

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Gelatin Pastils	430	Gloria Tonic	629
„ Styptic	981	Gloriosa Superba	859
Gelatina Sol. Steril.	424	Glossaries	640
<i>Gelatinum</i>	424	Glossinia Palp., Morsitans, 586 <i>et seq.</i>		
„ Calcii Chloridi, 5 to 7 Cc.	258	Gloves, Operation	270
„ Formalisat.	425	Gloves, Rubber...	270
„ Lamellæ Ophthalmic	539	Glucantha	813
„ Sterules	424	Glucarsenol	205
„ Zinci, and with Ichthyol, Pisic 5%, Resorcin 3%	829	Glucosan	758
Gelignite	575	Glucosazone	375, 377
Gelineau's Dragées, 1 <i>p.d.</i> in- creased to 3	157, 629	Glucosides	859, 165
'Gels'	363	Glucosone	651, 758
<i>Gelsemii Radix</i> , 5 to 15 gr.	425, 80	<i>Glucosum</i>	426 & 80
Gelsemin (Extractive), $\frac{1}{2}$ -2 gr.	426	Intrav. : 75 Gm. in 300 Cc. in 1½ hours.—L. ii./29, 723.		
Gelsemine	426	„ Gamina	646
Gelseminina, 1/100 to 1/32 gr.	426, 226	„ Media	617, 619
Gelesiminæ HCl., 1/60 to 1/20 gr.	426	„ Estn. in Blood 645 & <i>v.</i> Blood.		
Genasprin, 5 to 15 gr.	74	„ Surgical Dressing	428
General Paralysis, treatment by malaria inocu.	1080	„ Syrup	696
Genoscopolamine, $\frac{1}{2}$ mgr.	500	„ Tests for, in Urine	370
Gencydo...	859	„ Tryptic Broth	606
<i>Gentianæ Radix</i>	859	„ Sterules (for feeding)	427
Gentian Violet, 321, 273; Aniline	614	Glucusimide, <i>Glusidum</i> , $\frac{1}{2}$ to 2 gr.	754
Geraniol	166	Glukhorment	651
Geranium Mac., 1 to 5 gr., 859; Cape	871	Gluten, 591; Glutoid Caps.	698
Gerhardt's Test...	359	Glycaphorm, 1 to 2 dr.	566
German Chamomile, 840; Glos- sary	644	<i>Glycerin</i> , 1 to 2 dr.	429 & 80, 273
German Measles	996	„ <i>Acidi Borici</i>	10, 3
Germander	890	„ „ <i>Carbol.</i> 1 in 5	16
Germanin.	314	„ „ <i>Hydriodici</i> , 20 m.	41
Germanium	859	„ „ <i>Tannici</i>	95, 429
Germicides, Chapter on	262	„ Agar	619
Gerrard's Test Solution	375	„ Aloes	138
Ghati or Ghatti Gum	2	„ <i>Aluminis</i> (c. Acid Tan- nic, 430)	139, 426
Giardia	543	„ <i>Amyli</i> , 1 to 8	—
Gicmsa's Injection, 728; Stain,	575	„ Antiseptic Power	273
Gin	26	„ Atropinæ...	214
Gingelli Oil	876	„ Belladonnæ	225
Ginger	895	„ Bismuthi Nitratis	231
Gingerin, $\frac{1}{4}$ to 1 gr.	895	„ Bismuth. et Sod. Tart., 1 dr.	663
Gingerol	895	„ <i>Boracis</i> , 1 to 6	429
Ginseng	859	„ Broth	617
Gipsy Nut	892	„ c. Aq. Rosæ	430
Gitin, Gitalin	400, 72	„ Di-acetyl-morphinæ, 1 to 2 dr.	566
Glanders...	547	„ Di-iodo-hydrin	522
Glands Ductless, (<i>see also</i> Gland in question)	957, 175	„ Eastoni, 15 m.	420
Glandulæ Supraren. Sicc., 4 gr.	975	„ Ext. Bone Marrow, 1-2 dr.	958
„ Thyroideæ Sicc., $\frac{1}{2}$ to 4 gr.	988	„ Ferri Dialysat., 60 m.	415
Glandulen	961	„ „ Perchlor.	413
Glaser's Salt, 30 to 120 gr.	718	„ Glyceroph. Co., 1 to 2 dr.	39
Glass for Technical Work	778	„ „ c. Medulla Rub., 1 to 2 dr.	39
Glass, Soluble, or Water	778	„ Hyd. Perchlor.	468
Glauber's Salt	779	„ „ Alc. (<i>caution</i> not for administration)	468
Glaucium Luteum	859	„ Hypophosp., 1 dr.	692
Glauramine	322, 270	„ Iodoformi	508
Glaxo	590	„ Iodi (and Morton's) 512,	515
Glaxovo	591	„ Jelly, 430, 414; Micro	81
Gliadin	113	„ Pancreatis, 1 to 2 dr.	638
Glonoin Sol., $\frac{1}{2}$ to 2 m.	575			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Glycerin, Papain, 1 dr. <i>c.c.</i>	...	652	'Glycin,' 5; Glycine, 4;	...	887
" <i>Pepsini</i> , 1 to 2 dr.	...	662	Glycine Hispidæ,	4, 95
" Pessaries	431	Glycocoll, 10 to 30 gr.	...	430
" Phosphori= <i>Elix.</i> , 15	...	688	Glyco-gelatin and Pastils	...	860 & 94, 226
to 60 m.	...	706	Glycogen, $1\frac{1}{2}$ to 2 gr.	...	566
" <i>Plumbi Subac.</i>	...	751	Glycoheroin, 15 m. to 1 dr.	...	38
" Resorcin	...	430	Glycolactophos	...	433
" Rose Water	...	762	Glycopasta Aconiti, Bellad.,	...	372
" Soap Liq.	...	26	Hyoscy.	...	811
" Sodii Cinnam., 30 to	...	117	Glycosuria	...	165
60 m.	...	431	Glycothymoline	...	629
" Spirit	...	431	<i>Glycyrrhiza</i> , 5 to 20 gr.	...	566
" Substitutes	...	431, 801	Glycyrrhizin. Amm., $\frac{1}{2}$ to 5 gr.	...	433
" Suppositories	...	812	Glykaline	...	434
" Tampons	...	813	Glykeron, 15 m. to 1 dr.	...	365
" Tinctures, <i>vide</i> Gly-	...	380	GLYL :—	...	139
cetracta	...	420	Amygd. Ess. sine HCN.	...	295
" <i>Tragacanth</i>	...	158	Anethi; Anisi; Aurant.	...	1042
" in Urine	...	575	Amar.; Aurant. Flor.; Carui;	...	523
Glyc. Calf Lymph	...	952	Caryophylli; Cinnam.; Fœni-	...	559
Glyceritum Boroglycerini	...	10	culi; Lavandulæ; Limonis;	...	892
" Fe., Quin., Strych., 15 m.	...	420	Menthæ Pip.; Menthæ Vir.;	...	589
" Phenolis	...	16	Myrist.; Pimentæ; Pini;	...	858
Glycero-alcohol, 5-60 m.	...	430	Rosæ; Sassafras; Thymi;	...	426
" Piperaz, 5 to 10 gr.	...	703	Vanillæ	...	860
Glycerole Easton, 15 m.	...	420	Glymol=Paraff. Liq. <i>q.v.</i>	...	219
Glycerophosphates	...	36 <i>et seq.</i>	Gmelin's Test	...	958
Glyceroph. de Sod. Crist.	...	38	Gnoscopine	...	204
Glyceryl Antimonite	...	158	Goa Powder	...	533
" Carbonates	...	30	Goat Serum in Cancer...	...	218
" Trinit., $\frac{200}{50}$ to $\frac{1}{50}$ gr.	...	575	Goats and Leprosy, Edn. XVIII, p.	...	409
GLYCETRACTA :—	431 <i>et seq.</i>		Malta fever	...	712
" Aconiti, 0.4% alk., Av. 1 m.	...		Goat's Beard	...	219
" Bellad., 0.375% alk., 1 to 2 m.	...		Goat's Milk	...	491
" Calumbæ, 10-20 m.	...		Goat's Rue	...	869
" Cascara, $\frac{1}{2}$ to 1 dr.	...		Goitre, 517, 714, 775, 918;	...	845
" Catechu, 5 to 15 m.	...		and Therap. Ind.	...	623
" Chirettæ, $\frac{1}{2}$ to 1 dr.	...		Goitre and Iodine in Water	...	918
" Cinchonæ, 3% alk., 8 to 25 m.	...		Gokhru	...	860
" Cocæ, 0.25% alk., 1 to 2 dr.	...		Gold and Sodium Chloride	...	219
" Colchici, 0.5% alk., Av. 3 m.	...		" Beater's Skin	...	958
" Conii, 0.45% alk., Av. 3 m.	...		" Chloride, 218; Soln.	...	204
" Digitalis, 1 to 2 m.	...		" Colloidal	...	371, 533
" Ergotæ, 10 to 30 m.	...		" Cure	...	218
" Gelsemii, 5 to 15 m.	...		" for Syph. diagnosis	...	409
" Gentianæ, 15-30 m.	...		" "Cyanide"	...	712
" Hamamelid., 5 to 15 m.	...		" Treatment of Phthisis	...	219
" Hydrastis, 5-15 m.	...		" Sodium Thiosulph.	...	219
" Hyoscy., 0.075% alk. Av., 3 m.,	...		Golden Fire	...	629
" Ipecac., 1.1% alk., Expt., 1 to	...		Golden Seal, 10 to 30 gr.	...	491
4 m. Emetic, 30 to 40 m.	...		Gomenol and Pâte	...	869
" Jaborandi, 5-15 m.	...		Gomme Arabique 1, Sénégal 1,	...	845
" Krameriæ, 5-15 m.	...		Goutte	...	623
" Nucis Vomica, 0.75% Strych.	...		Gonal Capsules...	...	918
2-6 m.	...		Gonococcus, Vaccine	...	390
" Pruni Virg., 5-30 m.	...		" in Urine	...	548
" Quassia, 2 to 5 m.	...		" Culture Media	...	548
" Rhei, 5 to 30 m.	...		Gonorrhœa	...	918, 1064, 548
" Sarsæ, 2 to 4 dr.	...		" Mercurome in	...	483
" Scillæ, 1 to 5 m.	...		Goobar Nut	...	841
" Senegæ, 5 to 20 m.	...		Goose Grass	...	858
" Sennæ, $\frac{1}{2}$ to 1 dr.	...		Goose Grease	...	570
" Tarax., $\frac{1}{2}$ to 2 dr.	...		Gordon, on Cholera Vibrio	...	914
" Valerian, 5 to 20 m.	...		Gordon and Hine's Trypagar	...	532, 536
			Gordon's Panoptic Stain	...	400

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Gorit (Calc. Perox.), 3-10 gr....		259	Guaiacol (Cryst. 445) 1 to 5 m.		
Gossyp. Rad. Cort. ...		443	445 & 6, 225, 274		
Gossypium ...		435	„ Benz., 4 to 12 gr. .		447, 226
Gossyp. Arseniosium .		182	„ Cacodyl., $\frac{1}{2}$ -2 gr. ...		186
„ Camph. ...		264	„ Calc. Sulphonate ...		448
„ Capsici ...		273	„ Camph., 5-10 gr. .		447
„ Carbolisat. ...		16	„ Carb., 5 to 15 gr....		447, 226
„ Ferri Perchlor. ...		413	„ Cinnam., 5-15 gr. .		447, 226
„ Hyd. Iodidi ...		463	„ Iodide, 5 to 15 gr. ...		447
„ Hyd. Perchlor. 469,		471	„ -Iodine Oil. ...		446
„ Iodoformi ...		508	„ Pot. Sulphonate .		448, 70
„ Iodi, 6% ...		513	Guaiacyl ...		448
„ Menthol. ...		558	Guaicamphol. ...		447
„ Ol. Terebinth. ...		701	Guanidine, Guanin 944 & 174,		383
„ Sal Alembroth ...		472	Guarana, 10 to 60 gr. ...		861
„ Stypticum ...		413	Guaranine, 1 to 5 gr....		249, 861
Goulard's Extract ...		706	Guarea ...		851
Gout, 702; Powders, 878; <i>see</i>			Guaycuru, 861; Guaza ...		266
also Therap. Ind. ...		1065	Guimauve Pastils ...		431
Gouttes Ameres de Baumé			Guinea Worm ...		1065, 550
4 m. ...		599	Guipsine... ..		894
Gowland Hopkins' Method ...		389	Gum Acacia, 1, 2; Ghatti (Indic.)		2
Gowers' Hæmo. Solns... ..		396	„ Acac. Intravenous ...		1
Graham on Colloids ...		361	„ Chewing ...		850
Grains de Lin ...		867	„ Chicle ...		850
Gram's Method Solns. and Table		549,	„ Glucose ...		2
		614	„ Plant ...		444
Granati Cortex .		660, 661	„ Red ...		856
Grant's, Sir D., Inhalation and			„ Thus ...		699
Insufflator ...		289	Gun-Cotton ...		359
Grant's Sparteine Test ...		241	Günzburg's Capsule and Test		415
Granula Dioscoridis, 1 to 5 ...		181			
Granules Aconitine and Nitras,			Gurjun Balsam, $\frac{1}{2}$ to 2 dr. 843,		137
$\frac{1}{10}$ mgr. ...		100	Gut, Chromic, Iodised, etc. ...		541
Granules Atropine Sulph., 1			Guttæ Ac. Carbol., 17; Adrena-		
mgr. ...		213	lin, 977; Alum. Acet., 140;		
„ Digitaline Nat. ...		399	Atropinæ Sulph., $\frac{1}{4}$, $\frac{1}{2}$, 1 and		
„ Digitoxin, $\frac{1}{250}$ gr. ...		399	2%, 214; Atropinæ c. Co-		
„ Hyoscyamine, 1 hrly... ..		503	caina, 214; Atropinæ c. Zinco,		
„ Strophanthin, $\frac{1}{10}$ mgr. 790			214; Atropinæ et Quininæ,		
Grape Sugar ...		426	214; Castor Co. 1 dr., 848;		
Graves' Disease, <i>see</i> Goitre			Chlorof. cum Menthol Co.,		
Exophthalmic.			289; Cinnamon Co., 386;		
Gray's Stovaine Dextrin Inj....		352	Cocainæ Hydrochloridi (&		
Green, Brilliant ...		324	c. Adren.), 337; Cocainæ		
„ Malachite ...		323	Oleosæ, 335 (and Factory Act)		
Green Mountain Cure .		717	Cupri Sulphatis, 390; Da-		
Gregory's Pill = Pil. Coloc. Co.,			turinæ, $\frac{1}{4}$ %, 503; Dionin, 565;		
Gregory's Powder, 10 to 60 gr. 881			Eucainæ, 344; Hectine, 208		
„ Salt ...		139	Homatropinæ, 1%, (et c.		
Grenacher's Soln. ...		401	Cocaina), 217; Horsti 831;		
Grenz Rays ...		315	Hydrargyri Nitratis (Aural),		
Grey Oil, 2 to 3 gr. ...		455	467; Hydrogen Perox., 494;		
„ Powder, 1 to 5 gr. ...		454	Hyoscinæ, 0.5% (et c. Cocaina),		
Griffith's Mixture, $\frac{1}{2}$ -1 oz. =			498; Hyoscyaminæ, 503;		
Mist. Ferri Co. ...			Inosemzowi. 383; Iodi		
Grignard Reaction ...		548	Farrer, 1087; Morphinæ et		
Grindeline, 1 to 2 dr. ...		444	Cocainæ (Aural), 562; Physo-		
Grindelia .		444	stigninæ, 0.06 to 1% 693		
Griserin ...		319	(et c. Cocaina), 694; Physos-		
Grossich's Solution ...		519	tigminæ et Quininæ, 694;		
Ground Nut Oil .		841	Pilocarpinæ, 0.5%, 695;		
Groundsel ...		886	Quininæ Formatis, 2%, 727;		
Guaiaci Resina (& Lig.) 5-15 gr. 444			Rosæ, 2 to 10 m., 562;		
Tests for Blood ...		392	Sodii Arsenitis et Ferri, 5 m.,		

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
183; Zinci Chloridi (et c. Cocaina), 827; Zinc Chlorid (Aural), 827; Zinc Chlorid. c. Adrenalin, 827; Zinc. Sulphat 831.			Hardhack ...		852
Gutta-Percha and Tissue ...		271	Harrington, Thyroxin ...		985
Gutzeit's Test ...		36	Harmala, Harmine ..		861, 165
Guy's Tonic ...		629	Harmalin (Magenta) ...		320
Gwathmey's Synergistic Method		107	Harrington's Soln. ...		470
Gymnema var. ...		861	Harrison Federal Law ...		68
Gynocardia Odorata ...		605	„ T.B. Stain ...		599
Gypsum (Calcii Sulphas) ...		260	Hartley's Test ...		360
Haarlem Drops		702	Hartshorn and Oil ...		148
Hæmacytometers ...		395	Harvard Liquid ...		869
Hæmalum and Acid ...		401	Hashish ...		266 & 55
Hæmatein (Hæmatin) 861, 393, 401			Haust. Chloralamidi, 1 oz. ...		284
Hæmatoporphyrin 795 & 367			„ Co., 1 oz. ...		284
Hæmatoxylin, 861, 187; Stains 401			„ Copaibæ, 1 oz. ...		624
Hæmatoxyli Lignum ...		861	„ Creosoti, $\frac{1}{2}$ to 1 oz. ...		384
Hæmochromogen Test ...		393	„ Emeticus purgans, 1 oz. ...		166
Hæmoglobin and Caps, 1 to 2 dr. 582 & 394			„ Filicis, 1 oz. ...		423
Hæmoglobinometers ...		395	„ Imperialis ...		718
Hæmoglobinuria ...		508	„ Nitroglycerini, $1\frac{1}{2}$ oz. ...		577
Hæmolysin ...		896	„ Santonini et Ol. Ricini, $1\frac{1}{2}$ oz. ...		759
Hæmomanometers ...		402	„ Sulphonal, 1 oz. ...		795
Hæmoplastin ...		974	„ Terebeni „ ...		803
Hæmoptysis ...		154, 1066	„ Trional, 1 oz. ...		796
Hæmorrhage ...		1067	„ Ureæ Co., $3\frac{1}{2}$ ozs. ...		816
Hæmorrhagic Infective Jaundice 610			Hayem's Blood Fluid		396
Hæmorrhoids ...		449, 1067	„ Solution (Serum) ...		769
Hæmostatic Serum, 974; See also 253 <i>et seq.</i>			Hay "Fever, 919; Nebulæ ...		575
Haffkine's Cholera Prophylactic 913			„ Vaccines ...		920
„ Plague Vaccine ...		563	„ Reaction Outfit ...		920
Hafnium ...		58	(See also Protein Therapy and Therapeutic Index.)		
Hair Dyes, Amidol, 34; Copper, 34; Henna, 862; Hydrog. Perox., 494; Inecto, 308; Iron Tannate, 34; "One Solution," 34; Pot. Permang., 553; Mrs. Potter's Walnut Juice, 308; Pyrogallol, 34; Paraphenylene, 308; Silver ...		34	Hazel Foam and Comps. ...		448
Hair Lotion, Amyl Nit. and Pilocarpine ...		157	Head and Headache Powders		630
„ „ E. Wilson's... ..		149	Heal-All ...		852
„ „ Resorcin ...		751	Health Resorts... ..		459
Hair's (Dr.). Cure for Asthma ...		629	Heart, Auricular Fibrillation 393, 721		
Halazone Tablets ...		54	Heart Extract. Syph. Test ...		574
Haldane Oxygen App. ...		635	Heat as Antiseptic ...		278
Hallam Moss ...		786	„ Treatment, Radiant ...		314
Hall Edwards CO ₂ App. ...		23	„ Heather. <i>Syn. Erica Vulgaris</i> , <i>cf. Ericolin.</i>		
Hall's Testicular Agar... ..		549	Heberden's Ink, = Mist. Ferri Arom., '85, 1 to 2 oz. ...		208
Halliburton's Test ...		394	Hectargyre ...		208
Hall's Wine ...		629	Hectine, 0.1 to 0.2 Gm. ...		879
Halogens, Effect of. ...		254	Hedeoma ...		861
„ Quant. Separation. ...		153	Hedera and Hederin ...		481
Hamamelidin, $\frac{1}{4}$ to 2 gr. ...		449	Hegner's Test ...		
Hamamelidis Cort. et Fol. ...		448	Heiser's (Chaulmoogra) Injn. $\frac{1}{2}$ to 10 Cc. ...		606
Hamilton's Pill ...		381	Helalin, 852; Helba ...		857
Hammond's Remedy ...		35	Helcinin, $\frac{1}{4}$ to 2 gr. ...		863
Handkerchiefs, Aseptic ...		436	Helianthin ...		188, 418
			Helicon, 5-15 gr. ...		74
			Heliotropin ...		861
			Helium ..		336, 337
			Hellebore, Black, Green, 1-5 gr., White ...		893
			Heller's Test ...		363
			Hellige Colorimeter ...		369, 408
			Helmerich's Pomade ...		799
			Helonias dioica ...		862
			„ Compound, 1 dr. ...		862

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Hemisine	976	Honeysuckles	867
Hemlock (Lesser, 836)	381	Hookworm, <i>see</i> Ankylostom.		
„ Spruce, 878; Water...	...	851	Hopkins' Method	389
Hémostyl	974	Hop Smoking	868
Hemp, Canadian, 170; Russian	...	845	Hordenine	862
Henbane, 501; Egyptian 210,	...	502	Horder, Sir Thos., Cacodyl &		
Henna	862	Nuclein Injns.	187, 188	
Hepatic Abscess	529	Horder, Sir Thos., Immunogens	...	956
Herbe aux Chantres	856	Horehound, 30 gr.	869
Herogen, 2 dr.	583	Horlick's M. Milk tabs.	98
Heroin HCl., $\frac{1}{25}$ to $\frac{1}{2}$ gr.	566	Hormonal, 15 to 20 Cc., Chil-		
„ Addiction	567, 63,	639	dren less	974
„ in any proportion ㊦	63	Hormones (Pancreas 640) ...	964, 975,	175
Herpes and Chick. pox.	954	Hormotone Tabs.	989
Hervea (Herva Matte)	253	Horrock's Method	434
Hetol, 3 to 5 gr.	25	Horse-chestnut	835
Heusner's Glue...	869	Horse-hair	542
Hevea Brasiliensis	270	Horsenettle	887
Hexachlorethane	293	Horseplasma	973
Hexalin	294	Horseradish	852
Hexamina = Hexamethylen-tet-			Horse Serum	973
ramine, 5 to 15 gr. 450,	226		Horsley's Wax	849
„ Experiments with, 450			Horst's Eye Drops	831
and 81, 274; in			Horticultural Poisons 178, 997,	1000	
Cholecystitis, 100			Hort, on Life Cycle of Bacteria	...	951
grain doses	681	Hospitals and D.D.A.	1010, 1011	
„ Benzoate, 5 to 15 gr.	452	Hound's Tongue	854
„ Borate, 15 to 60 gr.	452	Household Ammonia	148
„ Camphorat., 8 to 12 gr....	...	453	Houseleek	886
„ Ethyl-Bromide	245	Hübl's Iodine Solution...	86
„ Glycochol	454	Huile Camphrée	263
„ Mercury Compds.	478	„ „ Sterilisée	263
„ Salicylate, 5 to 15 gr.	453	„ Creosot. Iodof.	507
„ Sod. Acet., 30 gr.	454	„ de Bouleau	705
„ Sodium Benzoate	453	„ de Cade	704
Hexanitrin, 1 gr.	409	„ de Foie de Morue	616
Hexavaccine	913	„ d'Iodure Mercurique,		
Hexyl-resorcin, 2 to 10 gr. 753,	226		1 Cc.	463
Hey's Green Paste	325	„ de Jusquiaume Co.	501
Hiera Picra, 3 to 10 gr.	138	„ d'œillette	619
High Explosives	307,	575	„ d'Olive Neutralisée	620
„ Frequency	312	„ de Pétrôle	659
Hill Diarrhœa	572	„ Grise Injectable, 2 to 3 gr.	...	455
Hill's (Leonard), Oxygen Bag	...	635	„ Lourdes de Pétrôle	655
Himrod's Cure	717	Hulle's Soluble Strychnine	...	794
Hindu Dates	890	Humbergum	625
Hippocastanum	835	Humagsolan	697
'Hippocras,' 895; Hippurates	...	8	Human and Humanised Milk	...	585
Hirudo	961	Humulus Lupulus	867
Hirudin	961	Hurtley's Test	360
Hiss Medium	608	Huxham's Tincture, $\frac{1}{2}$ to 1 dr.	...	297
Histamine, 406, 670, 673, 966 & 73			Hycol	33
Histidine	407 &	365	Hydatid Fluid	392
Hock	26	Hydnestryle	612
Hoffman's Anodyne, 60 to 90 m.	...	109	Hydnocarpus, <i>var.</i>	605, 611	
Hog Cholera	550	„ Eth. Esters.	612
Holarrhena	862	„ Anthelmintica	605, 612	
Holloway's Ointment & Pills	...	630	Hydnocreol	612
Holocaine HCl.	345,	226	Hydramyl, 660; Hydrangea	862
Homatropinæ HBr., 1/80-1/20 gr.	217,	228	Hydrargyrum	454 & 82	
„ HCl., 216; Salicyl., 1/80			„ Colloidal	375, 377	
to 1/20 gr.	216	„ Ionisation	288
Homatropine	211,	216	Hydrarg. Amalgam	457
Honey 83; Water	118	„ Extinctum	460

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

ME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
d. Amido-Acetas, $\frac{1}{2}$ gr.	5	Hyd. Sulphocyanidum	478
Ammoniat.	458	„ Sulphuret c. Sulph.	477
Ammon. Chlor. (Sal	(Sal		„ Tannas, $1\frac{1}{2}$ gr.	476
Alembroth)	472, 274	„ Thymol Acetas, $\frac{1}{2}$ to 1 gr.	477, 228
Arsanilas...	33	„ et Zinci Cyanidum	461, 274
Benzoas, 1/50 to 1/10 gr.	459	Hydrarsan, $\frac{1}{2}$ oz.	183
Bichloridum = Perchlori-			Hydrastin, 2 to 5 gr.	492
dum, 1/32 to 1/16 gr....	...	467	Hydrastina (Alk.), $\frac{1}{2}$ to 1 gr.	492, 34, 228
Bijodat (Biniodid)	462	Hydrastinae HCl., $\frac{1}{2}$ to 1 gr.	493, 34
Biniodidum, $\frac{1}{32}$ to $\frac{1}{16}$ gr.	462 & 33, 260, 274	Hydrastininæ HCl., $\frac{1}{2}$ gr.	493, 34, 228
Bisulphid. or Bisulphuret,			Hydrastis, 10 to 30 gr.	491 & 34
P.l. '51 = Vermilion...	...	477	Hydrazine	31
Bromidum, 1/16 to $\frac{1}{2}$ gr.	459	Hydrazobenzene	310
Carbolas, $\frac{1}{2}$ to 2 gr.	459	Hydriodic Ether	112
Chloratum mite	473	Hydrion Tablets (Mercuric		
Chloridum = Subchlori-			Chloride)	470
dum, $\frac{1}{2}$ to 5 gr....	...	473	Hydrobromic Ether	836
Chloridum Corrosivum	467	Hydrocephalus Test	64
„ Mite, U.S. = Subchlor.	...	473	Hydrochinon	863
c. Creta, 1 to 5 gr.	454, 32	Hydrochlorates Alc. Princip.		
Cyanidum, 1/20 to $\frac{1}{4}$ gr	459, 274	Opii	631
Exstinctum	456	Hydrocotyle Asiatica, 4 to 10 gr.	862
Glycocoll, $\frac{1}{2}$ gr.	5	Hydrocupreine	387
Imido-Succinas, $\frac{1}{4}$ to $\frac{1}{2}$ gr.	476	Hydrogen Borate	9
Iodas, $\frac{1}{2}$ to $\frac{1}{4}$ gr.	834	„ Ion Concent. of Blood	190
Iodidum Flavum	465	„ „ Indicators	187
„ „ (-ous), $\frac{1}{2}$ gr.	465	„ Liquef. App.	141
Iodidum Rub., 1/32 to	...		„ Peroxide, $\frac{1}{2}$ -2 dr. 15,	493 & 84, 274
1/16 gr.	462 & 250, 274	„ „ Solid	496
„ Viride, $\frac{1}{2}$ to 1 gr.	465	„ „ Borated	495
Lactas, $\frac{1}{2}$ gr. hyp., per os,	...		„ „ Mouth Washes	495
1/5 gr.	465	„ Transmutation of	337
Naphthol-Acetas, $\frac{1}{2}$ to 1 gr.	477	Hydrogenated Fats	37
Nitras	466	Hydrogenit	141
Nitroso-Nitrate	363	Hydrolete	141
Oleas	602	Hydrophobia	568
Oleatum, 5, 10, 20 & 25%	...		Hydropyrin	79
et (c. Morphina)	602	Hydroquinine HCl.	387
Oxidum (-ous)	475	Hydroquinone, $\frac{1}{2}$ to 5 gr.	363
„ Flavum	476	„ Developers	296
„ Rubrum, $\frac{1}{4}$ to 1 gr.	477	Hydroxylamine, HCl. & Sulph.	862
Oxycyanidum	460, 33, 274	Hydroxycodaine	139
Oxysulphas	476	Hydroxy-phenylethylamine	407, 982
Peptonas, per os, $\frac{1}{2}$ gr.,	...		Hydroxyphthalophenon, 2-5 gr.	677
hyp. $\frac{1}{2}$ gr.	467	'Hydroxyl,' 493; Group, effect		
Perchloridum (Wool, 469),	...		of	254
1/32 to 1/16 gr.	467 & 274	Hyoscina	496, 46, 35
Persulphas, 2 to 5 gr.	476	Hyoscinae HBr., 1/200 to 1/100	...	
et Potass. Iod., 1/16 to	...		gr. or less	498, 223
$\frac{1}{4}$ gr.	463, 83, 274	„ HCl. & HI., 1/200 to	...	
„ Tablets, 33; see also	...		1/100 gr. or less	500
„ Solubes Biniodide	465	Hyoscyami Folia, 3 gr.	501, 47, 85
Protoiodid, $\frac{1}{2}$ to 1 gr.	465	„ Mutic. Fol.	502
Rhodanidum	478	Hyoscyamina, 1/200 to 1/100 incr.	...	502, 46
Salicyl., $\frac{1}{4}$ gr.	472	Hyoscyaminæ HBr. et Sulph.,	...	
„ Neut., $\frac{1}{10}$ gr. incr.	473	1/200 to 1/100 gr.	502, 503, 228
Salicyl.-Arsonas	189	Hyper and Hypo. Thyroidism	991
Stearas	603	Hyperglycæmia	640
Subchloridum, $\frac{1}{2}$ to 5 gr.	473, 32	Hyperol	496
„ Duret's Form Cryst.	473, 32	Hypertonic Saline	768
Succinas, $\frac{1}{4}$ to $\frac{1}{2}$ gr.	475, 228	Hypervitaminosis	105
Succinimid., $\frac{1}{4}$ to $\frac{1}{2}$ gr.	476, 228			
Sulphas, Subsulph., 2 to 5 gr.	476			
Sulphidum.	477			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Hypnal	228	Indigo ; Carmine and comps.	62, 91,	228
Hypnogen	817	Indol Reaction	437
Hypnone, 1½ to 5 m....	...	832	Indoxyl	381
Hypnophore Group	254	Industrial Methyl. Spirit	120
Hypo and Hyperthyroidism	...	991	Inebriety 117, 119, 211, 297,	...	371
Hypobromite Sol.	387	Inecto	308
Hypochlorite ... 44 <i>et seq.</i> & 3	Infant Feeding ...	583 <i>et seq.</i>	...
„ Dakin's ... 49 <i>et seq.</i> , 8	„ in Tropics	588
Hypod. Injections. <i>See</i> Sterules.	„ Foods "A," "B," "C,"
„ Purgatives : Aloin. ... 138	„ and Cocoa	586
„ Apocodeine, 357 ; Colo-	„ Starch for	588
„ cynthin, 381 ; Hormonal 974	Infectious Diseases Table	996
„ Sterules, <i>see</i> Sterules.	Infra-Röntgen Rays	315
„ Syringes, etc., to sterilize	Influenza, 921, 1070 ; Vaccine,
„ Thymol Disinfectant.	908, 921 ; Bacillus,
„ Tabs., <i>v.</i> Tablets. Hypod.	921 & 550
Hypophamine	966	„ Infective Period	996
Hypophosphites ... 690 <i>et seq.</i>	„ Epidemiology	923
Hypophysis	965	„ Filtrable Virus of	923
Hypophysin	969	„ and pneumonia	923
Hysterionica	863	„ War Office Conf. Vaccine	...	921
Hysterol...	826	„ in India	922
Ibogaine and HCl., ½-½ gr.	863	„ Detoxicated Vaccine	923
Ice Cream	487	Infundibular Ext., ½ to 1 Cc....	...	968
Iceland Moss	849	Infundin	969
Ichthalbin, ½ to 15 gr.	505	Infusa Concentrata	505
Ichthoform	505	„ Alchemilla, 1 to 2 oz.	837
Ichthosulphol (Ichthyol)	503	„ <i>Alstonia</i> , ½ to 1 oz.	838
„ Ammon. Lith., Sod.,	„ * <i>Anthemidis</i> , 1 to 4 oz.	840
„ and Zinc Salts ...	504	...	„ * <i>Aurantii</i> , 1 in 20 (& * <i>Co.</i>),
„ Paste	505	„ ½ to 1 oz.
„ Proteinate	505	„ * <i>Buchu</i> , 1 to 2 oz.	845
„ Resorcin	505	„ * <i>Calumba</i> , ½ to 1 oz.	845
„ Salicyl	505	„ * <i>Caryophylli</i> , ½ to 1 oz.
„ Tampons	801	„ * <i>Cascarilla</i> , ½ to 1 oz.	848
Ichthyocolla	863	„ * <i>Chirata</i> , ½ to 1 oz.	851
Ichthyolate	503	„ <i>Cinch. Acid</i> , ½ to 1 oz.
Idozan	372	„ <i>Cocæ</i> , 4 to 8 oz.	332
Ignatia Amara Beans	599	„ Condurango, ½ to 2 oz.	852
Ihle's Paste	752	„ * <i>Cuspariæ</i> , 1 in 20, 1 to
Ilex Paraguayensis	253	2 oz.
Illipi (Nuts and Butter) ...	844, 164	...	„ * <i>Digitalis</i> , ¼ to ½ oz. ...	395, 72	...
Iminazolylethylamine ...	406, 78	...	„ <i>Ergotæ</i> , 1 to 2 oz.
Immune Body ... 896 & 580	„ Eupatorii, 1 to 4 oz.	857
Immunisation ... 896 <i>et seq.</i>	„ Gentiana Aromat.	859
Immunity Reaction	897	„ <i>Gentiane Co.</i> , ½ to 1 oz.	...	859
Immunogens	956	„ „ Conc. ...	506, 859	...
Imperial Drink...	718	„ Gokhru, 10 oz. daily	860
Incitamin	974	„ Hydrastis	492
Incubation periods of infectious	„ Kava-Kava, ½ pint	865
diseases	996	„ * <i>Krameria</i> , 1 in 20, ½ to 1 oz.
India Rubber ... 270 & 56	„ Lini, 1 in 30 ; Liquorice,
„ Paste for Mulls	56	1 in 90, <i>ad lib.</i>
Indian Hemp, Amer., 170 ;	„ * <i>Lupuli</i> , 1 in 20, 1 to 2 oz.
White, 842 ; <i>Indian Squill</i>	892	„ <i>Marrubii</i>	869
Indian Ink ... 576, 577	„ <i>Menyanthis</i> , 2-6 oz.	870
Indian Lemon Grass, 875 ;	„ <i>Polygalæ Co.</i> , ½-1 oz.	886
Licorice, 832 ; Pink Root,	„ * <i>Quassia</i> , ½ to 1 oz. ...	506, 880	...
888 ; Root ... 858	„ * <i>Rhei</i> , 1 in 20, ½-1 oz.
Indican ... 331	„ * <i>Rosæ Acidum</i> , ½-1 oz.	882
Indicator, Universal ... 190, 191	„ * <i>Scoparii</i> , 1 in 10, 1 to 2 oz.
Indicators for Vol. Analysis	...	187	„ * <i>Senegæ</i> , ½ to 1 oz.	886

*Also Conc., *i.e.*, 8 times strength, *v.* p. 505.

FIGURES IN HEAVY TYPE, *e.g.* **100**, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Inf. *Sennæ, ½ to 2 oz.	...	506	Inf. Cocaine et Sod. Bic.	...	339
„ *Serpentariæ, ½-1 oz.	...	886	„ (urethral)	357
„ Simarubæ, 1 oz.	...	887	„ Codeinæ Phosph. Hyp.,	...	381
„ Symphiti, 1 to 2 ozs.	...	889	„ 1 gr. in 15 m.	...	853
„ „ Conc., 2 to 4 dr.	...	889	„ Coninæ HBr., 1 to 3 m.	...	264
„ Tabaci	873	„ Curare Hyp., 1 to 6 m.	...	446
„ Uvæ Ursi, ½ to 1 oz.	...	841	„ Curschmann's, 15 m.	...	405
„ *Valerianæ, 1 in 40, ½ to	„ Durant's	406
1 oz.	„ Ergotæ Hyp., 5 to 10 m.	...	406
„ Vincæ Majoris, 5 oz.	...	894	„ Ergotoxinæ, 2 to 15 m.	...	345
„ Violæ Tricolor	894	„ Eucain, Lact. (urethral)...	...	27
Inhalatio Iodi Co.	...	386	„ Fibrocoumarin, 25 m.	...	446
Inhalation Allii Sativ....	...	838	„ Guaiacol (Durant)	446
Inhalations, Continual, 128, 385;	„ Guaiacol c. Iodoform	...	446, 520
Oro-nasal	385	„ Guaiacol c. Iodo et Camph.,	...	606
Inhaler, Ammon. Chlor.	...	146	„ 4 to 15 m.	...	217
„ Nasal Ozonic, Ozonic,	...	556	„ Heiser's	463
„ Poor Man's, Portable	...	386	„ Homatropinæ, 1 to 6 m.	...	460
„ Yeo's	260	„ Hyd. Biniodidi (vaginal)...	...	454, 1092
jections, To sterilise...	„ „ Cyan., 2 to 10 m.	...	455
INJECTIONS, HYPODERMIC:—	„ „ Intramusc., 10 m.	...	463
„ Acid, Carbol., 5-20 m.	...	17	„ „ „ Surg. Adams,	...	463
„ „ Chaulmoog. 'C'	...	613	„ 5 m.	...	460
„ „ Lactici (laryngeal)	55	„ „ Iodid., Ragazzoni, 2	...	471
„ „ Salicyl. (rectal)	65	„ to 6 m.	...	472
„ Adrenalin Co.	...	981	„ „ Iod. Intrav. Spittel...	...	475
„ Aluminis (Vaginal).	...	139	„ „ Lambkin, 10 m.	...	476
„ Alypin c. Suprarenin	...	345	„ „ Oxycyanid.	...	498
„ Antimonii (metal) Intra-	...	168	„ „ Perchloridi (Uterine	...	502
„ Antimonii Oxidi, 15 to	...	158	„ and Vaginal)	512
„ 30 m.	...	160	„ „ Perchlor. Intrav., Gt.	...	512
„ „ Ox. Fortior	...	161	„ „ Orm. Hosp., ¼ gr.	...	511, 512
„ Antimonii Pot. Tart. Castel-	...	166	„ „ Subchlor., 10 m.	...	508
„ lani, ½ to 1 Cc.	...	328	„ „ Succinimidi, ¼ to ⅓	...	508
„ Antimonii Sod. Tart.	...	183	„ gr.	...	508
„ Antipyrin, 8 to 30 m.	...	183	„ „ Hyoscina, 5 to 10 m.	...	540
„ „ et Cocainæ, 8 to	...	328	„ „ Hyoscyaminæ, 1/200 gr. inc.	...	822
„ 30 m.	...	357	„ „ Iodi. Hyp. Fortiss, 3 to	...	732
„ Apocodeinæ, 30 m.	...	171	„ 5 m.	...	557
„ Apomorph., 5 to 10 m.	...	174	„ „ Iodi, C.L.T.E. (also Douche)	...	562
„ Argenti Nit (urethral)	...	183	„ „ Carbolisati (Uterine)	...	562
„ Arsen. Iodid., 3 m.	...	183	„ „ Intravenous...	...	565
„ Arsen. et Ferri, 1 Cc.	...	184	„ „ Iodi Guaiacol et Camph.,	...	576
„ Arsen. et Strych., 5 to 10 m.	...	185	„ 4 to 15 m.	...	347
„ Arsen. et Strych. et Quin.,	...	214	„ Iodoformi (bladder)	...	281
„ 5 to 10 m.	...	211	„ „ Ætherea	...	606
„ Atropinæ, 2 to 8 m.	...	233	„ „ c. Guaiacol	...	694
„ Atrop. c. Strych.	...	633	„ „ c. Menthol	...	877
„ Bismuthi Subnitratiss	...	188	„ „ Iodolysin	...	696
„ Brou	...	251	„ „ Lecithin, 1 Cc.
„ Cacodylate Co., av. 17 m.	...	446, 520	„ „ Luminol-Sodium, ½ to 3 gr.
„ Caffeinæ Hyp., 1 to 6 m.	...	263	„ „ Mannitol-Quinine
„ Camph. Guaiacol & Iodine,	...	263	„ „ Menthol
„ 4 to 15 m.	...	263	„ „ Morphina Acet., 1 to 3 m.
„ Camphoræ Hypod., 10 to	...	263	„ „ et Atropinæ, 1 to 3 m.
„ 30 m.	...	263	„ „ Morphina Hyp., 5-10 m.
„ See also Sterules Hyp.	...	263	„ „ Nitroglycerin, 1 to 4 m.
„ „ Hyp. Æther, 10 m.	...	337	„ „ Novocain cum Suprarenin
„ Cocainæ Hyp. (5%), 5 to	...	337	„ „ Nuclein, 15 m.
„ 10 m., 338; Barts.	...	339	„ „ Ol. Chaulmoogr.
„ Cocainæ et Nitroglycerini	...	339	„ „ Physostigmin., 1 to 4 m.
„ up to 15 m.	...	339	„ „ Picrotoxini, 3 to 6 m.
			„ „ Pilocarpin Nit., 2 to 6 m.

*Also Conc., i.e., 8 times strength c. p. 505.

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Inj. Plumbi (vaginal)	706	Insulin Chem. Exn.	643
„ Pot. Permang. (vaginal) 553,	555		„ Clinical Experience	646
„ „ Permang (urethral) ...	553		„ Complications following ...	648	
„ Quin. HBr. Ac., $\frac{1}{2}$ to 1 Cc.	728		„ Contraindication ...	644	
„ „ HCl. Ac., 3 to 12 m.	730		„ Crystalline ...	643	
„ „ Intrav., 4 to 15 gr. ...	730		„ Distribution ...	642	
„ Ragazzoni, 2 to 6 m. ...	463		„ Diab. Trtment Simplified ...	649	
„ Sal-Alembroth, 10 m. ...	472		„ Excessive Dose ...	645	
„ Salinæ et Gum Acac. ...	1		„ from yeast, fish, etc., ...	642	
„ Salvarsan, 198; c. Novocain	200		„ Glucose Equivalent ...	648	
„ Sodi Arsenitis et Ferri No.			„ Glucose <i>per os</i> or intrav.		
1 and No. 2, 1 Cc. ...	183		with ...	645	
„ Sodii Arsen. et Strych.,			„ Hypoglycæmia ...	645	
5 to 10 m. ...	184		„ Injection Technique... ..	644	
„ „ c. Quin., 5 to 10 m....	185		„ Inunction of ...	646	
„ Sodii Cacodyl., 15 m. ...	188		„ in diab. coma ...	645	
(Hyp., Intrav.; & Rectal)			„ in Surgery ...	650	
„ Sodii Chloridi ...	767 <i>et seq.</i>		„ in various affns. ...	650	
„ „ Cinnamatis, 10% sol.,			„ Keeping props. ...	643	
30 to 60 m. ...	26		„ Oral Use ...	646	
„ „ Coumaratis, 25 m. ...	27		„ Patent ...	640	
„ „ Morrhuat., $\frac{1}{2}$ to 4 Cc.	618		„ Picric Acid Meth. ...	642	
„ „ Nucleinat. ...	281		„ Pituitary with... ..	647	
„ „ Salicyl., 15 to 30 m.	70		„ Refs., general ...	647	
„ Strychninæ, Arsen. Iod. et			„ Standard ...	644	
Quin., up to 1 dr. ...	793		„ Suitability of case ...	644	
„ Strych. Hyp., 5 to 10 m. ...	793		„ Tablets... ..	643	
„ „ Sulph., 1 to 6 m. ...	794		„ Units ...	643	
„ Suprarenal, 1 to 5 m. ...	981		„ Zymase ferments in		
„ Thecalis Anæsthetic ...	351		relation ...	646	
„ Thiosinamin et Phenazone,			Intarvin	651	
8 to 15 m. ...	765		Integar Caps. ...	858	
„ Thiosinamin c. Sod. Salicyl.,			Intemperance, <i>see</i> Inebriety &		
15 to 30 m. ...	765		Therap. Ind.		
„ Thorii Oxidi ...	807		Internol ...	657	
„ Zinc Chlor. (vaginal), 828;			Intestinal Pills, etc. ...	697	
Sulphatis (Vaginal) ...	831		„ putrefaction ...	533	
Insect Bites ...	1036		Intracardiac Injns. ...	980	
Insect Flowers, Dalmatian ...	880		Intramaine, Intramuscular, 1 to		
Insecticides, Horticultural, etc.	875,		5 Cc.	799	
„ Petroleum ...	659		Intravenous Dose Table ...	1106	
<i>See</i> also Cresol Soap Soln.,			Intra-spinal Anæsthesia ...	343, 351	
31; 'N.C.I.' 572; Therap.			Inula Helenium, 863; Inulin, 757,	863	
Index, Bites and Stings			Inulase ...	76	
and Parasites, Animal.			Invert Sugar ...	757 & 157	
Instruments, to Sterilize ...	260		„ „ Syrup ...	157	
„ Thymol Disinfectant... ..	810		Invertase ...	76	
Insufflatio Bismuth, et Morph.	236		Invigoroids ...	630	
„ Calcis Iodatis c. Bism.	834		Iod-cosin	188	
„ Eucalypti Gum. ...	856		Iodargol ...	379	
„ Iodoformi & Comps....	508		Iodatol ...	520	
„ Menthol (& Comps.) ...	557		Iodelkon ...	679	
„ Orthoformi c. Resorcin	346		Iodeol, 1 Cc. ...	379	
„ Paraformi ...	132		„ Caps. and Ovules	379	
„ Suprarenal ...	976		Iodex, and with Meth. Sal.	516	
Insufflator Drops ...	289		Iodia ...	639	
Insurance Scripts 639; and			Iodicin ...	622	
D.D.A., 1004, 1007, 1015, 1016,	639		Iodides Estn. ...	153	
INSULIN , 20 Units ...	640, 94		Iodine ...	510 & 85, 274	
„ Manufre. ...	670		„ Absorption Test... ..	361	
„ Aqueous Extret. ...	642		„ Albumen Comps. ...	522	
„ Blood Sugar Estn. 406-408			„ Colloid Sol. ...	371	
„ Cammidge on ...	647		„ Color Limits ...	86	
„ Chemical Composition	642		„ Comps., Organic ...	519	
			„ Douche	512	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Medicine for Livestock ...	716, 85, 86		Iodo-Ray Magnesium Sulphate		
„ Feeding Expts. with ...	716, 85,		with	685
„ Formalin Gut ...	541		„ „ Oral Use	680
„ and Goitre ...	715, 775, 918		„ „ Pills, 681; Intoler-		
„ in air ...	430		ance	681
„ „ Benzene ...	519		„ „ References, Oral	681
„ „ Dichlorethylene ...	292		„ „ „ Intrav.	683
„ „ foods... ...	429		„ „ Slipules 0·3 and 0·5		
„ „ Paraffin ...	519		Gm.	680
„ „ Soil ...	429		„ „ Sodium Content	679
„ „ Water (<i>see also Water</i>)			„ „ Stearettes, 0·3 and		
715, 755, 918, 422			0·5 Gm.	680
„ Intrav. Injn. ...	511		„ „ Sterility of Solns...	679
„ Iontophoresis of ...	236		„ „ Toxicity, 679, 682, 683, 146		
„ Isopropyl Alc. Soln. ...	87		„ „ Uses	679
„ Jelly ...	513		„ „ „ with Tolysin	685
„ 'Nascent' ...	517		„ „ „ X-Ray pictures	681
„ Numbers of Fats. ...	86		Iodo-Salicin	81
„ Organic Estimation ...	86		Iodostarin Tabs., 3 gr., 1 to		
„ Sterules (Skin) ...	518		3 t.d.	523
„ Iodol, 30 to 45 gr. ...	519, 228		<i>Iodum</i>	510 & 85
„ c. Ext. Malti, 1 oz. ...	520		<i>Iodum</i> , Collodial	371
„ Tablets ...	520		„ „ Oleatum, 10%	512
„ Iodol, 40% ...	87		Iohydrin	522, 228
„ Iodinosol ...	67		Ionic Medication	279
„ Iodised Gut, 541; Phenol and			Ionisation	253, 279
„ dil. Injn., 17; Salt, 714, 430 ;			„ „ Intensive Whitcombe		287
„ Sweets ...	715		<i>Ionium</i>	323
„ Iodised Wool, 6% ...	513		<i>Ionone</i>	894
„ Iodo-Acetone ...	832		Ions, Hyd. and Hydroxyl 187, 280		
„ „ Cyanine ...	317		Iontophoresis	279
„ „ Caffeine, 2 to 10 grains ...	252		<i>Ipecacuanha</i> , $\frac{1}{2}$ to 2 gr. exp.,		
„ „ -Casein ...	522		15 to 30 gr. emetic		523 & 89
„ „ Eosin ...	133		<i>Ipecine</i>	525
„ „ Fluorescein... ..	133		<i>Ipomœa. Orizabensis</i> et var....	864, 865	
„ „ -Glyc. Sol., 1 in 50 ...	512		Irradiation of Sterols	104
„ „ -iso-propyl-alcohol ...	522		Irradiated Oils	320
„ „ protein, 10 to 15 gr. ...	522		Ireland N., Poison Sched. ...	1003	
„ „ Tablets, 5 and			Iridin, <i>syn.</i> Irisin, 1 to 3 gr. ...	864	
10 gr. ...	522		Iridium (Collodial) ...	366	
„ „ -Tannin Syrup, $\frac{1}{2}$ to 2 dr....	513		Iris Florentina, Versicolor ...	864	
„ „ -theobromine, 2 to 10 gr....	806		Irish Moss ...	851	
„ Iodoform and Acetone, 509;			„ „ Free State Poisons		
and Eucal. Bougies ...	508		Schedule	1002
„ „ Benzoyl Chloride .	508		Iron Alum, 3 to 10 gr....	...	421
„ „ Bile Test ...	365		„ „ Collloid	372
„ „ Dressings ...	508 <i>et seq.</i>		Iron and Arsenic Drops, 5 drops		
„ „ Gauze Bandages .	508		(And Inj.)	183
„ „ Oil ...	507		„ „ Comps., Organic	415
„ „ Paste, 509; Pencils	509		„ „ in Foods	73, 79
„ „ Test for Acetone ...	360		„ „ Tannate Hair Dye	...	34
„ „ Varnish, 508; Petrolatum	509		<i>See also Ferrum.</i>		
„ Iodoform (& Præcip.), $\frac{1}{2}$ to 3 gr.			Irradiated Foodstuffs	596
507 & 275			Irritant Gases	1101
„ „ Aromat. ...	507		Isacen, 2 to 4 granules...	279
„ „ Tampons ...	801		Isatin	63
„ „ Iodol, 1 to 3 gr. .	510		Isinglass and Preps.	863
„ „ Iodolysin, Inj., Sol., Pigment	766		„ „ Japanese	836
„ „ Iodo-pyrrol ...	510		Islands of Langerhans	641
„ „ Iodo-Ray ...	679, 146, 275		Iso-amyl-amine...	982
„ „ „ Adrenalin with ...	681		Iso-amylene	839
„ „ „ Assay ...	679		Iso-caine	69
„ „ „ Duodenal Tube Method	682		Iso-Emetine	538
„ „ „ Intravenous Use ...	683		Isomeric Compounds	256
			Isomorphous Compounds	...	253

FIGURES IN HEAVY TYPE, *e.g.* **100**, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Isopral	...	294	Kaffir pox	...	955
Isopropyl Alc.	...	122	Kahn Syph. Test	...	583
„ Benzene	...	541	Kakodyle	...	185
„ Iodine	...	87	Kala Azar	159, 164, 168, 1073 &	551
„ Tinctures	...	124	Kalzana Tablets	...	56
„ Spirits	...	125	Kapok	...	436, 666
Isotonic Boric Acid Lotion	...	10	<i>Kaladana</i> , 865; Kalandura	...	854
Isotonic Cocaine Lotion	...	338	Kalmopyrin, 5-15 gr.	...	77
„ Quinine Injection	...	731	Kamala, 30 to 120 gr.	...	424
„ Saline Solution	...	767	Kangaroo Tendon	...	542
„ Sugar Solution	...	757	<i>Kaolin</i> , $\frac{1}{2}$ to 1 oz.	...	142
„ Sod. Bic. Solution	...	772	Kaolin, Colloidal	...	143
Isotopes	... xxxii., xxxiii.,	331	Kapok	...	436, 666
<i>Ispaghula</i> , 45 to 150 gr.	...	864	Kaputine	...	630
Istizin, 2 to 6 gr.	...	279	Kaposi's Ointment	...	571
Italian Glossary	...	645	Karox	...	631
Itrosyl	...	110	Kasak, 1 to 2 dr. (children),	...	
Ivy	...	861	adult $\frac{1}{2}$ oz.	...	278
Ixora, 30 to 45 grs.	...	864	Kasena, 1 dr. (children), adult	...	
Izal; Caps., Fluid	...	33, 264	$\frac{1}{2}$ oz.	...	278
Jabon , F.E.=Sapo	...		Kastanol, 835; Kat.	...	847
Jaborandi, 5 to 60 gr.	...		Katanga Radium	...	323
	694, 696 & 90		Kataphoresis; Kathions,	...	
<i>Jalapa</i> , 5 to 20 gr., 864; <i>Jalapæ</i>	...		Kathode	...	279
<i>Resina</i> , 2 to 5 gr.	864 & 160		Kauri Gum	...	865
Jalapin, Jalapurgin	...	864	<i>Kavæ Rhizoma</i>	...	865
Jam preservatives	...	493 , 500	Kaylene	...	143
Jamaica Dogwood	...	878	Kay's Preps.	...	631
James's Fever Powder...	...	630	Keating's Lozenges	...	631
„ Powder, 3 to 6 gr.	...	166	Keene's Cold Cure	...	631
Japan Wax	...	242	Kefir, 589; Kelene	...	110
Japanese Isinglass	...	836	Kelp, 510 & 85 ; Kelly's Paint	...	360
Jarabe (F.E.=Syrup) Brea	...	704	Kelpion	...	516
<i>Jasmine</i> , Yellow	...	425	Kepad	...	48
Jateorhiza Cal.	...	845	Kephir	...	589, 10
Jaundice, Epidemic	...	610	Kepler Malt and Oil	...	631
Jecovol	...	40	Keratin, 8 gr., and for Pills	...	697
Jelly Fish Stings	...	706	Kermes Minerale	...	157
Jenner Centenary Celebra-	...		Kernel Oil	...	151, 31
tions	...	954	Kernite	...	3
Jennerisation	...	952	Kerocain, 1/5 to 1 gr.	...	346
Jenner's Stain	...	398	„ with Adrenalin, Tabs. and	...	
Jensen's Modif. Gram Method	...	549	Sols.	...	346
Jephson's Powder, 60 gr.	...	797	Kerol and Caps	33, 534 &	264
Jequiritol Serum, Jequirity	...	832	Kerosene	...	659
Jesuit Tea	...	253	Ketone Group, effect of	...	258
Jeyes Fluids	...	33, 264	Kharsivan	...	194
Jerusalem Artichokes	...	758	Khat	...	847
John's Disease	...	551	Khoka	...	331
Jonnesco's Injections	...	353	Kidd's Strychnine Solution	...	793
Jorrison's Test	...	21	Kidney Extract	...	961
'Joule'	...	282	Kidney Tests	816 & 62 , 63 ,	385
Joulie's Phosphate 777; Ratios	...	382	Kieselguhr	...	144
Jubol Tablets	...	836	Kiliani Test	...	73
Juglandin, 2 to 5 gr.	...	864	Kinectine	...	208
Jujubes, 430; <i>see also</i> Trochisci	...		<i>Kino</i> , 5 to 20 gr.	...	865
'G'	...		„ <i>Eucalypti</i> , 5 to 20 gr.	...	856
Jumble Beads	...	832	Kineurine, 3 to 8 gr.	...	38
Juniper Tar Oil	...	704	Kjeldahl Estimation	...	381
Juniperus Com	...	865	Kleinenberg's Stains	...	401
Jungmann's Tooth Pdr.	...	888	Klondol	...	33
Juniperus Virginiana	...	848	Knob Root	...	852
Jusquame, 501; Jute	...	436	Knorr's Antipyrine	...	327
			Knyvett Gordon Stain	...	400
			Koch's Tuberculin	...	936

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Koko	631	<i>Lamella</i> — <i>contd.</i>		
Kola Nut, 10 to 20 gr....	...	252	{ Cocaine, 1-200 & 1-50 }		217
Koleradraaber	383	{ Homatrop, 1-200 & 1-50 }		
Kolynos Dental Cream	...	631	{ Cocaine, 1-200 gr. }		694
Koppeschaar's Sol.	4	{ Physostig., 1-1000 gr. }		
Koronium Bromide	788	Eucaine, 1-100, 1-50 gr. ...		344
Kossam Seeds	844	Gelseminine, 1-500 gr....		426
Kotex Sanitary Pads	...	436	Homatropine, 1-100 gr. (<i>B.P.</i>		
Koumiss	589, 10	'14)		217, 539
<i>Koussou</i> , $\frac{1}{2}$ to $\frac{1}{2}$ oz.	—	Hyd. Perchlor., 1-100.000 gr.		470
<i>Krameria</i> , 866; Krcatinin	...	368	Hyoscine, 1-500, 1-200 gr....		498
Kramer's Method	407	Hyoscyamine, 1-5000 gr. ...		503
Krapp Wurzel	882	Iodoform, 1-1000 gr. ...		509
Krebisote, 3 to 15 gr.	238	Morphine, (et c. Atrop., 1-		
Kreosote, 1 to 5 m. incr.	...	383	5000), 1-500 gr. ...		214, 562
Kresapol	33	<i>Physostigmine</i> , 1-1000 gr.		
Kresolum (and Liq.)	30	(<i>B.P.</i> '14), 1-500, 1-250 gr.		
Kryogenin (<i>vide</i> Cryogenin)	...				539, 694
Krysolgan	221	Pilocarpine, 1-500 gr. ...		696
Krystall Violet 321 & 271,	599, 605		Scopolamine, 1-500, 1-200 gr.		498
Kukui Oil	866	Silver Nitrate, 1-500 gr. .		175
Kurchi	536, 862	Thymol, 1-1000 gr. ...		811
L.E.S. Medium...	619	Zinc Sulph. (et c. Atrop.),		
			1-250 gr.		831
Labarraque's Liquor	45	Lamels, Medicated Gelatin, for		
Labdanum	866	use <i>per os</i>		539
Labelling of Poisons Order	...	1002	Laminaria Extraction, 85; Tents		866
Laburnum	854	Lamplough's Saline		631
Lacca, 887; Lachnanthes	...	866	<i>Lancæ Adeps</i>		100
Lacmoid, 91, 188; Lacrymal			Lancet C.A. Coefft.		263
Secretion, 767; Lactagol, 1			Lancets, Vaccination		953
dr., 443; Lacteol	57	Landsteiner's Law		995
Lactic Acid Bacilli Cultures, 57,			Langdale's Preps.		631
10; Liq., 57; Curdled Milk,			Langdon Brown's Mixture, 1 oz.		1053
58, 10; Added to Milk, 54,			Lange's Gold Test		533
587; Local use, 59; Suppes.			Langerhan's Islets		641
Vaginal, 59; Tablets	57	Lang's Bottle		214
Lactigen	57	Lanolin and Anhydrous, 100;		
Lactobacilline	57	Cream, 101; Ointment ...		101
" Glycogen	57	Lanolinum Hydrargyri .		457
Lactomaltine, 2 dr.	550	Lanosol Silver		380
Lacto peptine	631	Lanthanum		57
Lactophosphate de Calcium	...	56	Lapis Calamin. Præp., 829;		
Lactase	76	" Divinus		390
Lactose	866	Larkspur		888
Lactuca, Lactucarium, gr.	...	502	Lappa, 866; Larch Bark, 701;		
Ladanum	866	Lard		835
Ladenburg's Rule	254	Larix		701
Lævo-Pinene	148	Lassar's Paste		829
Lævo-Scopolamine	498	Lasiosiphon		866
Lævulose	757, 230, 379		Lathyrus .		867
" Test, Liver Efficiency	...	758	Laudanosine		139
Lambert-Towns Method	...	628	<i>Laudanum</i> , 5 to 30 m. .		630
Lambkin's Injections, 10 m....	...	454	" Sydenham's, 5 to 20 m.		631
<i>Lamblia</i>	543	Laughing Gas		146
<i>Lamellæ</i>	539	Lauri Fruct., Oleum		867
Adrenalin, 1-1000 and 1-500			<i>Laurocerasi Folia</i>		151
gr.	981	Lavandula		130
Alum, 1-250 gr.	139	Laverain Tabs., 5 or 6 p.d.		742
Atropine, 1-5000 and 1-500			Laveran's Stain		592
gr.	214, 539	" Staining Method ...		592
{ Atropine, 1-5000 to 1-50 }		214	Laville's Gout Cure		631
{ Cocaine, 1-200 to 1-50 }			Lawsonia		862
Cocaine, 1-100, 1-200 gr.:			Laxans		677
(<i>B.P.</i> '14) 1-50; 1/20 gr. 338,		539	Laxatol, Laxen, Laxoin		677

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Laxamel...	657	Lichens	91, 92
Laxar, 1 to 2 dr..	...	658	Licorice	860
Lead Poisoning	705 & 149	" Indian	832
" Colloidal	372, 1043	Ligatures <i>var.</i>	541
" Guaiacolate	707	Light Green	325
" and Lead Selenium Com-	Light Treatment	278, 321
pounds in Cancer	372, 374,	511, 515, 530	Lightning Stroke	1105, 312
" Absorption, Test for	...	150	Lignum Rhodii	875
" Paint Regulations	...	149	Ligroin	660, for T.B.	601
" Salts as Antiseptic	...	275	Lilac Artificial = Terpeneol
" Tetra Ethyl, 659,	151 ;	...	Lily of the Valley	852
in Cancer	531	Lime Salts, Therapy ...	255 <i>et seq.</i>	...
" Iodid Coll.	374, 1043	Limnatis	961
" Phosph. Coll.	374, 1043	Limonade Purgative; Rogé	...	545
League of Nations <i>re</i> Cocaine,	Limonene, 10 to 20 m.	...	867
Opium, etc.	334, 627	<i>Limonis Syr.</i>	867
Lebertran	616	" cort vitamins	103
Lecanora	91	Linct. Ammon. Brom., 1 to 2 dr.	...	145
Lecithin, 3-5 gr. (and Powder,	" Apomorphinæ c. Codeina
10 to 15 gr., 541), 539 & 90,	230	...	1 dr.	172
Lecitogen, 3 to 4 dr.	540	" Bart's 1 dr.	629
Leclanche Cell	283	" Camph. Co., 1 dr.	629
Leeches, 961; Leek	838	" Codeinæ, 1 to 2 dr.	357
Leek, House	886	" Diamorph., 1 to 2 dr.	566
Lefroy's Crude Oil Emulsion...	...	659	" Expectorans, $\frac{1}{2}$ -1 dr.	158
Legal's Test	359	" Gee's, 1 dr.	629
Leishmania Infns. Antimony in	" Heroin, 1 to 2 dr.	566
158, 164, 1073; <i>see also</i>	551	" Mentholis, 1 dr.	557
Leishman-Donovan Bodies	552	" Morph., 1 dr.	562
Leishman's Stain	398,	558	" Morph. Hydrocyan, 1 dr.	...	562
" Wright's Modif. ...	399	...	" Opiatus, 1 dr.	629
Leistikow's Bougies	177	" Pini Terp. Heroin, 1 dr.	...	701
Lemco Meat Wine	632	" Scillæ, 1 dr. (and Co.)	629
Lemon Grass, 875; Juice, 593;	" " Opiatus, 1 dr.	629
Syrup	867	" Terp. Pini et Heroin, 1 dr.	...	701
Lenigallol, 65; Lenirobin	295	" Thymi et Diaphorm, 1 dr.	...	892
Lenitive Electuary	886	" Tolu c. Opio, 1 dr.	629
Lentine	308	Lindenblüthen	506
Leprosy, Bacillus	553,	554	Liniment, A.B.C.	98
" Chaulmoogra in	606	<i>Linim. Aconiti and Co.</i>	...	98, 20
" Etiology, Diagnosis 553,	554	...	" Aconiti et Chlorof.	98
" Potassium Iodide in ...	555	...	" Æruginis	389
" Recent Clinical Work	" Album, 700; <i>Ammoniacæ</i>	...	148
with	609	" Atropinæ	215
" A self-healing disease	612, 555	...	" <i>Belladonnæ</i>	225
" Vaccine Treatment	613	" " Æthereum	227
<i>See also</i> Therap. Ind.	1073	...	" Dil. L.I.P.	225
Leptandrin, 1½ to 2 gr....	...	867	" Bellad. c. Chlorof.	225
Leptospira, 610 ; in Water, 439,	442,	...	" Betulæ Co.	73
" Icteroides	613	" Boeckii	706
Leucin	95,	365	" Calaminæ et Co.	830
Leucite	152	" <i>Caleis</i>	260
Leucocytes; Leucocytosis	396	" <i>Camphoræ et Ammon.</i>	262, 263	...
Leucocytozoon	575	" Cantharidis Co....	...	269
Levigations	814	" Capsici (and Dx.)	273
Levisticum Officinale	867	" Carron	260
Levulose	757	" Chloral Co.	283
Levre Medicinale	279	" <i>Chloroformi</i>	290
Levy-Bing Lafay Syringe	455	" Crinale	268
Lewisite...	36	" <i>Crotonis</i>	875
Libanol	849	" <i>Hydrargyri</i>	456
Lice, to Kill	1081, 1082	...	" " Oleat. c. Morph.	602
Lichenoids, 1 or more	849	" Iodi, syn. <i>Tinct. Iodi</i>
			<i>Fortis</i>	514
			" Jaborandi	696

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Linim. Long's	700	Liq. Battley, 5 to 10 m.	...	629
" Menthol (& Co.)	557	" Bellostii is similar to	...	
" Methyl Aspirodine	...	86	Millon's Reagent	...	363
" Meth. Salicyl	73	" Berberidis Conc., $\frac{1}{2}$ to 1 dr.	...	844
" Myristicæ	872	" Bismuth. Ammon. Cit., 30-	...	
" Opii, 629; Picis	705	60 m.	...	229, 48
" Potass. Iod. c. Sap.	...	716	" Bismuthi Conc., 15 to 30 m.	...	229
" Ravogli	17	" Bismuth. Sed., 1 dr.	...	229
" St. John Long	700	" " Tartratis, $\frac{1}{2}$ to 1 dr.	...	239
" Salicyl (Methyl)	...	73	" Bituminis	300
" Saponis	762	" Bromi	...	388
" Simplex, L.I.P....	...	225	" " Arsenitis, 1 to 5 m.	...	181
" Sinapis	764	" Bromo-Chloral Co., $\frac{1}{2}$ to 2	...	
" Stokes'	700	dr.	...	283
" Succini Co.	889	" Calcii Chloridi, 15 to 45 m.	...	258
" Terebinth.	700	" Calcis, 1 to 4 oz.	...	260
" " Acet.	700	" " Chlorinat.	...	45
" Zinci Spissum	828	" " Lactat., $\frac{1}{2}$ to 2 oz.	...	56
Linseed and Oil	...	867	" " Lactoph.	...	56
Lintum Ac. Carbol, 5%	...	16	" " Sacch., 15 to 60 m.	...	260
Lintum Stypticum	...	413	" Calumbæ Conc., $\frac{1}{2}$ to 1 dr.	...	
Lints	...	436	(B.P. '89).	...	
Linum Usitat	...	867	" Caoutchouc...	...	270
Lipase (Lipolytic Ferment)	...		" Carbonis Deterg. ...	299, 275	
429, 637, 763 & 76, 77	...		" Carmini, 40 gr., 1 oz.	...	847
Lipiodol	520, 88	" Carnis	...	582
Lipoids	541, 91	" Caulophylli et Pulsatillæ, 1	...	
Lipoiodine	...	523	to 2 dr.	...	848
Liqueur de Labarraque	...	45	" Chiratæ Conc., 1 in 2, $\frac{1}{2}$ to	...	
Liq. Acid. Chromici	...	833	1 dr. (B.P. '98).	...	
" " Chrom.-Aceto-Osmici	...	834	" Chloromorph., 5-15 m.	...	290
" " Hypochlorosi Comp.	...		" Cocci	...	847
(Eusol)	...	46	" Cocainæ HCl. (Inj.), 5-10 m.	...	338
" " Osmici, 2-10 m.	...	834	" " et Antipyrin	338
" " Salicyl....	...	66	" Copaibæ, $\frac{1}{2}$ to 1 dr.	...	624
" Adrenalini Hydrochloricus,	...		" " c. Buchu et Cubeba,	...	
10 to 30 m.	...	977	1 to 2 dr.	...	625
" Alkalinus. Brandish	...	709	" Copaiba et Buchu et	...	
" Aluminii Acetici	...	140, 275	Cubebæ c. Santal, 1 to	...	
" " Aceto-Tart.	...	141	2 dr.	...	623
" " Chloridi	...	141	" Cresol Sap.	31 & 6, 264, 275	
" Aluminii Formatis	...	141	" " Co. U.S.X.	...	31
" Ammonice, 10 to 20 m.	...	148	" Creosoti, av. 2 dr.	...	384
" " Domest.	...	148	" Cuspariæ Conc., 1 in 2, $\frac{1}{2}$...	
" Ammon. Fort., 3-6 m.	...	148	to 1 dr. (B.P. '98)	...	—
" " Acet., 2 to 6 dr.	...	149	" Digitalis ad usum intern.,	...	
" " " Fort., '85, 25-75 m.	...	149	max. 45 m.	...	396
" Ammon. Anisat.	...	860	" Digitalis pro Inj., max. 5Cc.	...	396
" " Aromat.	...	150	" Donovan, 5-20 m.	...	183
" " Cit., 2 to 6 dr....	...	150	" Eastoni pro Syrup, 419;	...	
" " " Fort., '85, $\frac{1}{2}$ -1 $\frac{1}{2}$ dr.	...	150	ditto sine Ferro	419
" Antihystericus, $\frac{1}{2}$ -1 dr.	...	842	" Epinephrin, 0.5 Cc.	...	978
" Antim. Chlor.	...	33	" Epispasticus	...	269
" Antirheumatic, 30 m.	...	358	" Ergotæ Ammon., 10-60 m.	...	405
" Antisepticus, 1 dr.	...	10	" Ethyl Nitritis, 15 to 60 m.	...	110
" Argenti Nitratiss	...	175	" Euonymin et Cascara, $\frac{1}{2}$ to	...	
" Arsenicalis, 2 to 8 m.	...	180	1 dr.	...	410
" Arsenici Bromatus, 1 to 5 m.	...	181	" " et Iridin, $\frac{1}{2}$ to 1 dr.	...	410
" " HCl., 2-8 m.	...	181	" " et Pepsini, $\frac{1}{2}$ to 1 dr.	...	411
" Arsen. et Hyd. Iodidi, 5 to	...		" Ferri Acet., 5-15 m.	...	416
20 m.	...	183	" " Albuminati, 1 to 4 dr.	...	415
" Atropinæ Salicyl	213	" " et Ammon. Acet., 4 dr.	...	416
" " Sulph., 1%, $\frac{1}{2}$ to 1 m....	...	214	" " Dialysat., 10 to 30 m.	...	414
" Auri Ars. Brom., 5 to 10 m.	...	218	" " Hypoph. Fort., 10 to	...	
" Auri Hyd. Brom., 5 to 10 m.	...	218	30 m.	...	691

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Liq. Ferri Iodidi, 4 to 8 m.		417	Liq. Potassii et Sodii Hypo-		
„ „ Oxyd. Sacch., $\frac{1}{2}$ oz. ...		415	chloritum, $1\frac{1}{2}$ to 2 Cc....		46
„ „ Pept. (c. Quin., 416),			„ „ Permang., 2-4 dr. ...		—
1 to 4 dr. ...		415	„ pro Spirit. Amm. Arom. ...		150
„ „ Perchlor., 5-15 m. ...		414	„ pro Syr. Eastoni ...		419
„ „ Fortis, 1 to 4 m. ...		413	„ Quassiae Conc., $\frac{1}{2}$ -1 dr. ...		880
„ „ Pernit., 5-15 m. ...		415	„ Rhei Conc., $\frac{1}{2}$ to 1 dr.		
„ „ Persulph. ...		—	(B.P. '98). ...		—
„ „ pro Syr. Easton ...		419	„ „ Dulc., 1 to 3 dr. ...		401
„ „ Sesquichlor. ...		414	„ Rosæ Dulcis ...		876
„ „ Subsulphat., 3 to 6 m. ...		421	„ Santali c. Buchu et Cubeba,		
„ „ Tersulphat. ...		421	1 to 2 dr. ...		623
„ Ferro-Mang. Pept. c. Hæmo-			„ „ Co., 1 to 2 dr....		623
globin, 1 to 4 dr. ...		416	„ „ c. Kava, 1 to 2 dr. ...		623
„ Flavus ...		16	„ Sarsæ Co. Conc., 2-8 dr. ...		884
„ Fluoresceinæ ...		678	„ Sedans, $\frac{1}{2}$ to 1 dr....		493
„ Formaldehydi (& Sap.) 126,		130	„ Senegæ Conc., $\frac{1}{2}$ -1 dr. ...		886
„ Fowleri, 2 to 8 m. ...		180	„ Sennæ Conc., $\frac{1}{2}$ -1 dr. ...		—
„ Gelatin Sterilisat. .		424	„ Sennæ Dulcis, 1-3 dr. ...		886
„ Glonoin, $\frac{1}{2}$ to 2 m. .		576	„ Seriparus ...		661
„ Gutta Percha ...		295	„ Sodii Arsenatis, 2-8 m. ...		185
„ Humamelidis, $\frac{1}{2}$ to 3 dr. ...		448	„ Sodæ Chlorinat., 10 to		
„ Helalin c. Pepsin et c. Cas-			20 m. ...		45
cara, 1 dr. ...		852	„ „ Chirurg. U.S.X. ...		50
„ Hoffmann ...		109	„ „ Carbolatis ...		17
„ Hyd. Nitrat. Acid. ...		466	„ „ Ethylatis ...		774
„ „ Perchlor., $\frac{1}{2}$ -1 dr. ...		468	„ „ Hydroxidi, U.S., 5% ;		
„ Hydrarg. Antiseptic ...		470	P.G.V., 15% ...		—
„ Hydrogenii Perox., $\frac{1}{2}$ to 2			„ „ Hypobrom. ...		387
dr., 493 ; Estn., etc. 84			„ „ Methylat. ...		774
„ Hyoscine HBr., 3 to 15 m. ...		498	„ „ Stillingie Co., 1 dr. ...		888
„ Hypophysis, $\frac{1}{2}$ to 1 Cc. ...		968	„ „ Strych. HCl., 2-8 m. ...		793, 123
„ Iodi (Co., U.S., 513). ...			„ „ Testicularis, 15-30 m. .		982
„ (B.P. '85, 513) Fortis ...		514	„ „ Thymol, 1 in 800 ...		811
„ Iodo Ferro Mang. Pept., 1			„ „ Thyroidei, 5 to 15 m. ...		987
to 4 dr. .		416	„ „ Assay ...		171
„ Jaborandi, 5 to 15 m. ...		696	„ „ Tolu pro Syrup ...		843
„ Kramerie Conc., $\frac{1}{2}$ to 1 dr.			„ „ Trinitrini, $\frac{1}{2}$ to 2 m. ...		576
(B.P. '98). ...		—	„ „ Violæ Glucosidi, $\frac{1}{2}$ oz. ...		894
„ Mag. Bicarb. 1 to 2 oz. ...		545	„ „ Zinci Chloridi ...		827
„ „ Cit., av. 12 oz. (div.)... 545			Liquores Concentrati ...		867
„ „ Morphine Acet., 10 to 60 m. ...		562	Liquorice, 860 & 165.; Com-		
„ „ Bimec, 1.45%, 5 to 40			pound Powder of, 60 to 120		
m. ...		564	gr., 860 ; Liquorice (Indian). ...		832
„ „ HCl., 1%, 10-60 m....		563	Listerine, 1 to 2 dr. ...		10
„ „ Tart., 1%, 10-60 m. ...		565	Lister's Antiseptic ...		461, 1099
„ „ Natrii Silicici ...		778	„ „ Carb. Bdgcs. ...		16
„ „ Nitroglycerini, $\frac{1}{2}$ -2 m. ...		576	Litharge .		707
„ „ Opii Sedativus, 5-10 m. ...		629	„ „ Lithiated Sorghum Co.” ...		887
„ „ Pancreatis, 1 to 2 dr. ...		633	Lithii Aceto-Salicyl, 5 to 15 gr. ...		79
„ „ Pancreaticus, 1-2 dr. ...		638	„ „ Benzoas, 2 to 10 gr. ...		542
„ „ Papain et Iridin, 2 to 4 dr. ...		652	„ „ Borate ...		293
„ „ Pectoralis, 1 dr. ...		860	„ „ Bromid., 5-15 gr....		542
„ „ Pectoral Benzoic .		860	Lithii Carb., 2 to 5 gr. ...		542
„ „ Pepsini et Caff., 2 to 4 dr. ...		663	„ „ Citras, 5 to 10 gr., 542 ;		
„ „ Pepticus, 1 to 2 dr. .		662	Effervesc. (and Lax.)		
„ „ Picis Carbonis, 299 ; Ligni ...		300	1-2 dr. ...		543
„ „ Pierotoxini, 2 to 12 m. ...		877	„ „ Formas, 1 to 5 gr. ...		35
„ „ Pituitarii, $\frac{1}{2}$ to 1 Cc. ...		968	„ „ Glyceroph., 3-10 gr. ...		38
„ „ Plumbi Lactat. ...		706	„ „ Guaiacas, 2 to 5 gr. ...		543
„ „ Plumbi Subacet., Dil., Fortis ...		706	„ „ Hippuras, 5 gr. incr. ...		543
„ „ Potassæ, 10 to 30 m. ...		709	„ „ „ Eff., 1 dr. ...		543
„ „ Potass. Arsenat. et Bromid.,			„ „ Iodidum, 1 to 5 gr. ...		543
1 to 5 m....		181	„ „ Phenyl-cinchoninate ...		319
„ „ Potass. Arsenit., 2-8 m....		180	„ „ Quinas, 5 to 15 gr. ...		726

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Lithii Salicylas (Eff., 1 to 2 dr., 543), 5-20 gr....	...	543	Lotio Excitans	751
„ Sulphas, 5 to 10 gr.	543	„ Hyd. Acetica, 469; Biniodidi, 465; <i>Flava</i> , 468; <i>Nigra</i> , 475; Perchlor., 469; c. Acid. Carbol., 469; c. Ol. Tereb.	469
„ Sulpho-Ichthyolas, 10 to 30 gr. daily	504	„ Hyd. Zinc. Cy.	462
„ Tart. Acid., 5-20 gr.	543	„ Krameria Co.	7
Lithion, $\frac{1}{2}$ to 1 dr.	543	„ Paraffini Co.	660
Lithium	542	„ Parasiticide	469
„ Diuretin, 5-15 gr.	806	„ Picis Carb. Alk. et Arom.	299
Litmus Paper, Sol.	91, 138	„ Pilocarpinae (hair)	696
Liver Abscess ...	529 & 556		„ Plumbi Detergens	299
„ Diet	962	„ „ Evaporans...	707
„ Desicc., 5 gr. incr.	962	„ „ et Opii	706
„ Extract, $\frac{1}{3}$ to 1 table-spoonful daily	962	„ „ Lact.	706
„ Fluke ...	275, 423		„ Plumbi Spirituosa	707
„ Function Test, 146; <i>et seq.</i>	611	„ „ Tale et Amyli	706
„ of Sulphur	709	„ Pot. Thymatis	811
„ Tests ...	758, 147, 148		„ pro Acne ...	830, 881	
„ „ Van den Bergh	611	„ pro Capite	888
Livingstone Rousers	740	„ pro Mannibus	430
Lloyd, V. E., on syphilis—L. June 30/28, 1820.		„ Proflavine	307
Lloyd's Reagent	374	„ Quassia	880
Lobelia and Lobeline	544	„ Quininæ HCl.	728
Lobeline HCl., $\frac{1}{3}$ gr.	544	„ Resorcini (and Co.)	751
„ Sulph. Tabs., $\frac{1}{20}$ gr.	544	„ „ et Ac. Borici	752
Lockyer's Hair Restorer	632	„ „ et Acid Salicyl	751
Locock's Wafers	632	„ „ Pilocarp. et Canth.	752
Locke's Solutions	767	„ Rubra	831
Loeffler's Meth. Blue, 538; Serum	535	„ Salox	495
„ Pigment (Diph.)	413	„ Sod. Hyposulph....	...	94
Loew's Theory	251	„ Staphisag.	888
Loewi's Test	171	„ Sulphatum	831
Logwood	861	„ Sulph. et c. Sapone	798
London Paste	709	„ „ Co....	...	798
Longevity	154	„ Zinci Chloridi	328
Lonicera <i>var.</i>	867	„ „ Sulphatis	831
'Lords and Ladies'	841	Lotion Ammoniacale Camphrée	...	263
Loretin	319	Lovage	867
Lotio A.B.C.	98	Lowndes Cream; <i>vide</i> Cremor	...	
„ Acid. Acetici	4	Lozenges, Bases for, 814; <i>See</i> also Trochisci	...	
„ „ Benzoic	6	Luatol	242
„ „ Borici, 4%	10	Lubricant Glyc. Jelly	430
„ „ c. Zinc Sulph.	10	Lubricant Surgical	16
„ „ Carbolici (et c. Co-caina)... ..	15, 16		Lubricating Oils	659
„ „ Citrici et Phenolis	29	Luetin Skin test for Syph., Edn. XVIII.	...	
„ „ Hydrocyan. c. Sodio	44	Lugol's Solution = Liq. Iodi, '85, 5 to 10 m.	513
„ „ Picric, 1%	62	Lumbar Anæsthesia ...	343, 351	
„ „ Salicyl. c. Borace	66	Lumbricus, 759 and Therap. Index.	...	
„ „ Tannic Sulph.	95	Luminal, $\frac{1}{2}$ to 5 gr. ...	822 & 230	
„ Ætheris Composita	109	„ Tablets, $\frac{1}{2}$, $\frac{1}{3}$, 1 and $1\frac{1}{2}$ gr. ...	822	
„ Alba McKenna	831	„ Sodium. $\frac{1}{2}$ to 3 gr. ...	822	
„ Ammonii Chloridi	145	„ Tablets, 1 gr. ...	822	
„ „ et Cantharidin	269	„ in Epilepsy ...	822	
„ Balsami Peruvian	843	Luminous Paints ...	333	
„ Bismuthi	235	Lunar Caustic 174; <i>Mitigated</i> , <i>Toughened</i>	175
„ Boeck	706	Lundie's Tuberculin	946
„ Calaminæ et Oleosa	830	Lund's Oil	16
„ Calcii Sulphurat..	261	Lupulin (Lupulus, 2 to 5 gr.)	867
„ Calcii Iodat.	834			
„ Capillaris	751			
„ Crinalis	283			
„ Evaporans	122, 145			

FIGURES IN HEAVY TYPE, *e.g.* **100**, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Lycoperdon Gig.	868	Mag. Sulphas Exsicc.	548
Lycopodium	868	„ Sulphate Cream	547
Lycryl, 33; Lyddite	13	„ Sulphis, 10 to 30 gr.	93
Lymph, Calf, Glycerinated	952	Magnesium 545 & 92 ; Ions.	...	288
Lymphatic Gland Tabs., 5 gr.	963	Maguey	879
Lysidine	454	Maidis Stigmata, 868; Ustil-
Lysiform	275	lago, 868; Maize Ergot, 868;
Lysol 31, 32, 33; Assay 6, 264, 275	Oil	619
„ Martindale	32	Maize, 839; Oil 100, 490, 491
Lytta, $\frac{1}{16}$ gr.	267	Malachite Green 323, 230, 275
M.L.D. =Minimum Lethal dose			Malabar Fibre	542
73 & Vol. I., xxxii., xxxiii.	Malarene	157
Ma Huang	855	Malaria, <i>v.</i> Ther. Ind., 1075;
McConkey's Broth, etc. 436, 437	Etiology, 556, 557 ;
Mac Crorie's Stains	605	General Refs., 749; Cin-
McDade's Succus, 1 dr.	888	chonine in, 724, 744;
McDonagh's Preps.	316, 799	in England, Measures
Mache Unit	336	against	748
McIlheney's Br. Method	87	„ Inter-Health Board on	...	743
Mackintosh Paste	762	„ Plasmochin in	750
„ Sheeting	271	„ Quinidine & Cinchoni-
Mackenzie's Cure, 632 ; Eye-	dine in ...	719, 723	...
wash	469	„ Relapses	747
MacLagan's Test	67	„ Sir R. Ross on...	743
Maclean's Blood, Exn.	406	„ Treatment of Paralysis	1080	...
Madeira	26	„ Types and Parasites 557, 558
Madame Rachel	18	„ Staining Methods 558
Madder	882	„ See also Quinine ...	743	...
Magenta, $\frac{1}{2}$ to 4 gr., 320; Acid... 598	Male Fern (& Caps.) ...	422, 80	...
Magisal, 5 to 15 gr. ...	79, 16, 230	...	Malignant disease, Radium in	340	...
Magisterium Bismuthi	233	<i>et seq.</i>
Magnesia Cream, 1 to 4 dr	546	Malignant Œdema	559
„ Mixture	92	Malignant Purpuric Fever	909
<i>Magnesia Levis</i> and <i>Pond.</i> , 30	Malignant Pustule ...	906, 505	...
to 60 gr., 5 to 20 gr. rep.	545	Mallein	547
Mag. Acetyl-Salicyl, 5 to 15 gr. 79, 16	Malonal, <i>Malonurea</i> , 5 to 10 grs.	817, 275	...
„ Benzoas, 5 to 15 gr.	7	„ Identification ...	202, 230	...
„ Borocit, 15 to 30 gr.	11	Malt, 548; Assay of	92
„ Bromid., 10 to 20 gr.	245	„ Incompts. with	549 & 93	...
„ Cacodylas, $\frac{1}{4}$ gr.	186	„ Extract, 1 to 4 dr.	548
„ Carb. <i>Levis.</i> , <i>Pond.</i> , 30 to	„ „ Liq., 1 to 4 dr.	549
60; 5 to 20 gr. rep.	545	„ and Cascara, 1 to 4 dr.	550
„ Chaulmoograte	609	„ „ Hæmoglobin, 1 to 4 dr.	550	...
„ Chloras	545	„ „ Hypophosph. (and
„ Chloridum, 30 gr. or more	...	545	with Oil), 1 to 4 dr.	550	...
„ Citras Ver., 30 to 120 gr.	Malta Fever	559
„ Formas, 3 to 10 gr.	35	„ „ & Cholera, etc.
„ Glyceroph., 3-10 gr. ...	38, 7	...	„ „ Vaccines	949, 560	...
„ Hydrox., 5 to 120 gr.	545	Maltaffin and combinations, 1 to
„ Hydrox., c. Carbone, 1 to	2 dr.	549
2 dr.	546	Malted Glyceroph., 1 to 4 dr....	...	40
„ Hypochlorite	50	Maltine and Preps., 1 to 4 dr....	...	549
„ Hypophos., 3-10 gr.	691	Maltoferrose, 1 to 4 dr.	550
„ Lactas, 15 to 60 gr.	546	Maltolivine, 2 to 4 dr....	...	620
„ Oleas	604	Malva	506
„ Peroxid., 15 to 60 gr.	496	Mammary Gland	963
„ Pyrophosphas	92	Manaca	868
„ Ricinoleas, 1 to 4 dr.	621	Mandelin's Reagent	204
„ Salicyl, 10 to 30 gr.	67	Mandioca	839
„ Silicas	144	Mandl's Pigment	513
„ Sulphas, $\frac{1}{4}$ - $\frac{1}{2}$ oz.; 30-90	Mandragora	868
gr. rep. ...	546 & 275	...	Mandrake, 868; American	707
„ Sulphas Eff., $\frac{1}{2}$ -1 oz.; 60-	„ English = <i>Bryonia dioica</i>
180 gr. rep.	548	<i>q.v.</i>

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Manganese Colloidal	374	McCrorie's Stains	605
Mangan. Brom., 1 to 6 gr.	245	Meadow Saffron	357
„ Butyrat	551	Mead's Maltose	551
„ Citras, 3 to 5 gr....	...	552	Measles ...	996, 1075,	560
„ Ferro Phosph., 3 to 10 gr.	552	Meat Extracts, 581 <i>et seq.</i> ; Juice	581, 582	
„ Glyceroph., 1 to 5 gr.	38	„ Formalin Detection	30
„ Hydrat. Colloid	365	„ Preservation SO ₂	18
„ Hypoph., 1-10 gr.	552	Mechoacan	864
„ No. in Cascara	56	Meconine	139
„ Ox. Præcip., 3-10 gr.	552	Meconin-Morphine-Narcotine	569
„ Phosph., 1 to 5 gr.	552	Medicated Dressings	438
„ Sulph., 2 to 10 gr.	552	„ Wines	623
Manganese Thyroid Treatment	...	553	Medicine Stamp Acts, 624 ;	...	
Manna, 1 dr. to 1 oz.	868, 3	Concession	624
Manihot	839	Medinal, 5 to 10 gr. ...	319 &	232
Manilla Grain	841	Mediterranean Fever	559
Manioca	839	Medullary Glyccride, 1-2 dr.	958
Mannitol (Syn. Mannite)	869	Meglin's Pill	502
„ Nitrate Tabs., 1 gr. 409, 232	...		Meinicke's Reaction	533
„ Quinine, 1 to 2 Cc. hyp.	...		Melaleuca. ...	845,	869
(?)	133, 732	Mélange de Bonain	334
Manson's Stain	559	<i>Mel Depuratum</i>	93
Mantoux Test	947	„ Rosatum	882
Manures, Artificial	47	Melampyrite	607
Maran = Bals. Copaibæ	—	Melanuric Fever	508
Maranta	814, 869	Melia Azadirachta	842
Marchi Reaction	394	Melinite	13
Margarine	490, 491	Melioidosis	548
„ Vitamins in... 490	...		Melissa Off.	870
Margosa Seeds	842	Mellitum Mercurialis from M.	...	
Mariahuana	266	Annua v. FR. CX.	
Maricol, 1 to 4 dr.	621	Melograno	860
Marienbad Salt & Tabs., 60 gr.	780	<i>Melon Pumpkin Seeds</i>	853
„ Tab. (vegetable)	139	Melting Points of Fats	248
„ Antiobesity Tabs.	780	Meltzer's Lubricant	16
Marigold = Calendula	845	Membroids, 524; Memoranda V.I. xxx	...	
Marine Soaps	158	Menciere's Solutions	508
Marjoram.	876	Mendeléeff's Periodic Table xxxvi	...	
Markets, Drug, Ldn.—C.D. June 30/28, 851.	...		Mene Towels	436
Marmite	280 &	506	Meningitis, Cerebro-Spinal 909, 1045	...	
Marris' Atropine Test	604	„ Serum	912
Marron d'Inde	825,	835	„ Conf. on Standn. of Serum 912	...	
Marrow, Glyc. Ext.	958	Meningococcus, 910, 532; Cul-	...	
Marrubin, 1 to 2 dr.	958	ture Media, 911; Swab for 911	...	
„ Compounds	958	Menstruation, Diapers of Cotton,	...	
Marrubium, av. 30 gr.	869	436; Moss	786
Marsh Mallow, 506, 838; Pastils,	...		Mentha Piperita et Viridis	870
431; Marsh's Test	37	Menthofax	73
Marylebone Cream	597	<i>Menthol</i> , ½ to 2 gr. 556 & 133	...	
Massicot	707	„ Camphora et c. Phenol... 556	...	
Mastiche Test for Syphilis	410	„ Paraffin Caps	557
Mastich Leaf Oil	869	„ Plaster	557
Mastisol	869	„ Snuff, 557; Spray 557;	...	
Matches	688	„ Wool, 558; Valerianate 558	...	
Maté	253, 52	„ Synthetic	558
Matricaria Chamomilla	840	Mentholeate, 557; Menth-	...	
Maubeere, 882; Mauve (Malva) 506	...		Phenol	557
Mauveine HCl.	461	Menyanthes	870
May Apple	707	Merbaphen	491
May Weed	841	Mercaptan	795
May-Grunwald Stain	400	Merchandise Marks Act.	623
Mayer's Phenolphthalin Test... 412	...		Mercurettes	456
Mayer's Reagent	33	Mercurial Cream, 10 m. ... 454, 455	...	
„ Stains	401	„ Injections Intrav. 455, 471	...	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Mercuric Ammon. Chloride ...		458	Mercury Vapour Lamp ...		315
„ Benzoate, $\frac{1}{50}$ to $\frac{1}{10}$ gr. ...		459	Mescal Buttons		840
„ Biniodide, $\frac{1}{32}$ to $\frac{1}{16}$ gr. ...		462	Mesembryanthemum ...		870, 165
„ Iodide Soaps, 465; Hex-amine Compds. 478; Wool ...		463	Mesentery Gland ...		963
„ Nitrate Ointment ...		466	Mesothorium ...	325, 334, 351, 354	
„ Oleate and Comps. ...		602	'Meta' ...		126, 370
„ Oxide Yellow, 476; Red ...		477	Meta-benz.-carbazine ...		8
„ Oxysulph. ...		476	„ cresol ...		30
„ Potass. Iodide, 1/16-1/4 gr. ...		463	„ -dihydroxybenzene ...		750
„ Rhodanide ...		478	„ -phenylene diamine and HCl. ...	308 & 370,	419
<i>Vide also Hydrarg.</i>			Metag ...		729
Mercurius Dulcis ...		473	Metagen		598
Mercurochrome " 220 " 479, 84, 232, 275			Metaldehyde ...		126
<i>See also Mercurome.</i>			Metal Alloys as Pyrometers ...		261
Mercuro Zinc Cy., 461; Band-ages, Cream, Gargle, Gauze, Paste, Wool, etc, 462 <i>et seq.</i>			Metallix Tubes ...		292
Mercuriol ...		281, 456	Metals, Action of Acids on ...		177
MERCUROME ...		479, 84	„ Colloidal		361
„ Bactericid. Actn. ...		490	Metallic Oleates. ...		601
„ Balfour on Dose in plague, etc. ...		485	Metarsenobillon ...		41, 44
„ in undulant fever 487, 489			Metatone ...		103
„ Bougies ...		480	Metchnikoff's treatment ...		57, 10
„ Chemical Characters ...		480	Methanal ...		126
„ DiphenylCarbazid. Test ...		490	Methanol ...		24
„ Dose		479, 488	Methenamina, 5 to 15 gr. ...		450
„ Dudgeon on Dose ...		479, 488	Methyl-acetanilide, $\frac{1}{2}$ -2 gr. ...		3
„ Gauze ...		480	„ Acetyl-Iodo-Salicylate ...		85
„ Gonorrhœa ...		483	„ Alcohol ...		119 & 25
„ Hypersensitiveness		490	„ Aldehyde		126
„ Idiosyncrasy ...		490	„ Amidobenzaldehyde (p.) ...		365
„ Incompatibilities ...		480	„ Amidophenol, HCl. ...		296
„ Intravenous Use ...		483	„ Arsine ...		38
„ Introduction ...		489, 490	„ Amino-oxy-benzoate ...	345, 232	
„ Ionised Mercury in... ..		84	„ Amino-phenol-sulphate... ..		481
„ Ointment ...		480, 484	„ Aspidrodine. ...		85, 232
„ Oral Use ...		489	„ „ Balm ...		86
„ Pharmacology ...		479	„ „ Capsules, 5 and 10 gr. ...		87
„ References ...		481, 488	„ „ Liniment ...		86
„ Septicæmia ...		486	„ „ Pigment ...		87
„ Skin Antiseptic ...		480	„ Atropine Brom. and Nit. ...		216, 217, 232
„ Stains, to remove ...		480	„ Benzol ...		312
„ Sterules ...		480	„ Benzoyl Ecgonine ...		333
„ Surgical Use		480	„ Chloridum ...		870
„ Toxic Effects ...		489	„ Codeine Bromide, $\frac{3}{4}$ gr. ...		357
„ Uses ...		480	„ Cupreine ...		387
„ Vesical Injection ...		482, 483	„ Cytisine		848
Mercurosol ...		473	„ Ditannin ...		96, 232
Mercurous Chloride, 473; Iodide, 465; Lactate, 465; Nitrate, 466; Oxide ...		475	„ Eosin = Prime rose in Dye industry. ...		95
<i>Vide also Hydrarg.</i>			„ Glycocol		325
Mercury Amalgam ...		457	„ Green ...		251, 254
„ and Arsenobenzol ...		199	„ Group, effect of ...		883
„ Biniodide failed to sterilize gut... ..		260	„ Heptyl. Ketone		9, 500
„ Colloidal		375	„ Hydrobenzoate ...		4
„ Comps. Organic ...		490	„ Hydro-Cupreine HCl. ...		387
„ Hexamine Salts ...		478	„ to 12 gr. ...		30
„ Ions ...		288	„ -hydroxybenzene		113
„ Isotopes of ...		xxxiii	„ Iodide ...		541
			„ Isopropyl benzene ...		85
			„ Iodo-Aspirinate		883
			„ Morphine = Codeine, <i>q.v.</i> ...		580
			„ -nonyl-ketone ...		188, 418
			„ Nitrate ...		
			„ Orange ...		

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Methyl-Phenol	30	Milk Boiled <i>v.</i> Unboiled	587
„ phenylehinolincarb.	319	„ Boric Acid in	480
„ parahydrobenzoate	9	„ Broth	548
„ phenyleinehoninat.	319	„ Casein	466
„ propyl-phen. Hexa hyd.	556	„ Certified ...	464, 469,	470
„ psychotrine	538	„ Cellular elements in	483
„ -protocatechuic Ald.	892	„ Citrated ...	580,	773
„ Red	183	„ Clean	471
„ -Salicyl, 5 to 15 m.	72	„ Colostrum	466
„ Sedasprin...	88	„ Condensed ...	588,	423
„ Stannic Iodid.	163	„ Copper in	481
„ Sulphonal, 10 to 20 gr.	796	„ County Councils and In- spection	475
„ -Theobromine	249	„ Cows, slaughter of ...	472,	477
„ Thioninæ HCl.	325	„ and Cream Regulations...	480
„ Violet	320	„ Critical Temp. of	485
„ Xanthines ...	249,	805	„ Culture Medium...	619
Methylated Spirit (Mineralised and Industrial) 119 <i>et seq.</i> 28			„ Curdled ...	58,	10
„ „ Drinking ...	119,	28	„ and Dairies Act...	467
„ „ Regulns., N. Ireland... ..	28		„ „ „ Amendt. Act	468
Methylene Azur	576	„ „ „ Order	463
„ Blue, 1 to 4 gr. & Stains 325 & 61, 232, 275, 598			„ Designated ...	469,	470
„ „ Polychrome	393	„ Direct supply, Thermo- isolated...	463
„ „ Chloride	870	„ Dried ...	583,	483
Methylene-di-salicylic Iodide... ..	510		„ Drugs in	201
Methylenum Cœruleum ...	325		„ Fat 464 ; Fever	560
Methylic Alcohol	119		„ Foods ...	583 <i>et seq.</i>	
Methynol ...	27		„ Formalin in	480
Methylsal Balm	72		„ and Glycerophosphate ...	37	
Metol, 308 ; Developer... ..	236		„ Goats ...	589	
Metramine, 5 to 15 gr....	450		„ Grade A ...	585,	469
Metrie Wts., etc., xxxviii <i>et seq.</i>			„ Household	464
Meulengracht Test ...	612		„ Human ...	585,	489
Mezereum, 8 gr. ...	870		„ Hypersensitiveness ...	676	
Mianin ...	51		„ Injns. Steril., 5-10 Cc. intram....	...	676
Microbene ...	33		„ Inspection ...	467 <i>et seq.</i>	
Micrococcus Catarrhalis ...	908		„ Irradiated in rickets.— C. Watson, etc., L.ii./29, 704.		
„ „ Gonorrhœæ... ..	548		„ Lactic acid Added to ...	54,	587
„ „ Melitensis, <i>see</i> Vae- eines and... ..	553		„ Lactometer	466
„ „ Meningitis	910		„ Lactose	465
Microsporon Audouini & Furfur	570		„ Leithin	466
Microcosmic Salt ...	777		„ Licenees	469
Microscopic Media, ...	614		„ Mineral matter	466
„ Varnish ...	869		„ Min. of Agriculture on... ..	478	
Microcurie ...	336		„ National Conf. ...	585	
Midges, To kill ...	1036,	556	„ Pasteurised 587, 469, 470, 472		
Migraine Powders ...	252 & 630		„ „ „ Danger of ...	475	
Migraine, 8 to 15 gr. ...	252,	232	„ „ „ Detection of... ..	474	
Migralgin, 8 to 15 gr. ...	252,	232	„ „ „ Pasteurisers	473
MILK ...	464		„ „ „ Peptonised	639
„ Agar ...	543		„ „ „ Pox	955
„ Albumin ...	467		„ „ „ Preparations	583
„ Analysis ...	464		„ „ „ Preservatives	480
„ Aphthous ...	486		„ „ „ Prices, London	471
„ Arsenic in ...	201		„ „ „ Refrigerated ...	483 <i>et seq.</i>	
„ Artificial Human ...	585		„ „ „ in Sealeones	473
„ Asses' ...	467		„ „ „ Separated ...	467,	477
„ Average Composition 464, 466			„ „ „ Sewage in	487
„ Bacterial Reduction by Pastn., 473			„ „ „ Skimmed...	467
„ Bacteriological Exmn. ...	487		„ „ „ Solids, 464 ; Non-fat	465
„ „ „ Medium ...	619		„ „ „ Sour ...	58,	10
„ „ „ Standards of Graded 470			„ „ „ Souring of ...	58,	481, 488

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Milk	Special Designations		Mist. Antim. et Pot. Iod. (Cas-		
	Order, 469; Scotland...	469	tellani), 1 oz.	161
"	Specific Gravity...	464	" Antiseptica, $\frac{1}{2}$ oz.	777
"	Sterilised... ..	587	" Antispasmodica, $\frac{1}{2}$ oz.	788
"	St. Ivel Lactic	59	" Apomorphine Luff.,		
"	Sugar	866, 465	$\frac{1}{2}$ oz.	172
"	Survey of the Problem...	482	" Arsenii Quininae et Ferri		
"	Synthetic, 887, and see		$\frac{1}{2}$ to 1 oz.	181
	Edn. XVIII., p. 588		" Arsenii et Hydrargyri Iodidi		
"	Thermo-isolated	483	cum Phenazono, $\frac{1}{2}$ oz.	183
"	Tubercle Bacilli, Detec-		" Aspirin, $\frac{1}{2}$ oz.	76
	tion of 487, 601		" Asthmatica, $\frac{1}{2}$ oz.	788
"	" " Extent of		" Bacelli, $\frac{1}{2}$ to 1 oz.	181
	infection with 474, 483,		" Balsam Co., 1 oz.	7
	485, 595, 596		" Basham, 4 dr.	416
"	" Bacilli Thermal		" Belladonna, Xanthoxyli et		
	death-point 473		Hyoscy., 6 to 8 mins.	226
"	Tuberculin Tests	471	" Bismuthi, 1 oz.	228
"	Tuberculosis Order, '25 .	471	" Bismuth Astring, 1 dr.	228
"	" " Animals		" " c.pepsina, 1 to 2 dr....	...	230
	'slaughtered under 472,	477	" Bismuthi, Phenolis et		
"	Unsweetened Condensed	483	Morph., 1 oz.	230
"	'Upper'	583	" Boro-Benzoeat., 1 oz.	7
"	Vacuum bottles for	485	" Broadbent, $\frac{1}{2}$ oz.	739
"	Variation in	465	" Bromidi et Digitalis, $\frac{1}{2}$ to		
"	Veterinary Inspectn. 475,	476	1 oz.	711
"	Opinion on 478, 479		" Brominol c. Nuc. Vom.,		
	(See also Cream.)		$\frac{1}{2}$ oz.	245
"	Whey Powder	588	" Butyl-Choral, 1 oz.	247
"	Wooldridge, Prof. on	483	" Calc. Chlorid., $\frac{1}{2}$ oz.	258
Miller's Mouth Wash		7	" Calcii Hypoph., 1 oz.	691
Milliampere		282	" Calc. Lact., $\frac{1}{2}$ to 2 oz.	56
Millicurie... ..		336	" Camphoræ, 262; Conc.	172
" detruires		350	" Capsici Sed., $\frac{1}{2}$ oz.	273
Milne's Battiste		435	" Carminativa, $\frac{1}{2}$ oz.	895
" Eucalypt. Inunction		614	" Cascara, 1 dr.	278
Millon's Reagent		363	" " Co., $\frac{1}{2}$ to 1 oz.	278
Milton		50	" Catarrhalis Anti- 1 $\frac{1}{2}$ oz.	...	149
Mineral Naphtha	120, 659		" Chest, 1 dr.	860
Mineralised Meth. Spirit ...	120		" Chlori c. Quin., 1 oz.,		
Mineral Waters	427 447		(Yeo's), 737; Rose-		
Minchin's Garlic Preps.	838		berry's	738
Mineral Acids Sale	1000		" Cholera, 1 oz.	383
Minium=Red Lead	707		" " Tomb's Ess. Oils,		
Minot & Murphy Diet... ..	962		$\frac{1}{2}$ dr.	1046
Mirbane	310		" Copaibæ, $\frac{1}{2}$ to 1 oz.	625
Miré	845		" Creosoti, $\frac{1}{2}$ to 1 oz.	384
Mistletoe, 10 to 60 gr.	894		" " Co., 2 dr.	385
Mist. Ac. Aceto Salicyl, $\frac{1}{2}$ oz....	76		" Creosoti et Potass. Iodid.		
" Ætheris, c. Ammon., $\frac{1}{2}$ oz. ...	109		$\frac{1}{2}$ oz., <i>quartis horis</i> 384,	714	
" " Camph, 1 oz.	109		" <i>Cretae</i> , $\frac{1}{2}$ to 1 oz.	253
" Agrimonie Co., $\frac{1}{2}$ oz.	837		" Damianæ Co., 1-2 dr.	854
" Alba, $\frac{1}{2}$ to 2 oz.	548		" Dewees' Emmenagogue,		
" Ammoniaci, $\frac{1}{2}$ to 1 oz.			$\frac{1}{2}$ oz.	138
" Ammon.Brom. Phenazoni			" Diarrhœa, Bd. Hlth., 1 oz.	...	383
et Caffeinae, 1 oz.	145		" Diuretica, 1 oz.	709
" Ammon. c. Ether, 1 oz....	109		" Dysmenorrh., $\frac{1}{2}$ oz.	710
" Ammon. Picratis, $\frac{1}{2}$ oz....	64		" Eserinae Co., $\frac{1}{2}$ oz.	694
" Amygdalæ, $\frac{1}{2}$ to 1 oz.	152		" Ergotæ Alkalina, 1 oz.	406
" Anodyna, $\frac{1}{2}$ oz.	563		" Ergotæ Sedativa, 1 oz.	405
" Anticachexia, No.1, 2 & 3,			" " Co., $\frac{1}{2}$ oz.	406
1 oz.	747		" Essential Oils, $\frac{1}{2}$ dr. ...	1046	
" Anticatarrhalis, 1 $\frac{1}{2}$ oz.	149		" Exalgin, 2 to 4 dr.	3
" Anti-cholERICA, 1 oz.	383		" Febrifuga, $\frac{1}{2}$ oz.	149
" Anti-dipsom, $\frac{1}{2}$ oz.	211, 297		" Ferri Aper., 1 oz.	414

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
ist. Ferri Aromat., '85, 1 to 2 oz.			Mitigated Caustic	...	175
" " Arsen., $\frac{1}{2}$ -1 oz.	...	414	Modelling Wax	...	655
" " Co., $\frac{1}{2}$ to 1 oz.	...		Molasses	...	5, 870
" " Salicyl, 1 to 2 dr.	...	67	Molecular Wt., effect of	...	256
" " Salina, 1 oz.	...	414	Mollin, <i>var.</i> , 870; Molybdenum,		
" Filicis, 1 oz.	...	423	421; Molybdenite, 421;		
" Gentianæ Alk., 1 oz.	...	859	Momordicin	...	855
" <i>Guaia</i> ci, $\frac{1}{2}$ to 1 oz.	...		Molybdic acid	...	356
" Guaiacol, 1 oz.	...	445	Monarda	...	809
" c. Quinina, $\frac{1}{2}$ to 2 dr.	...	445	Monazite	...	807 & 57, 351
" Hepatica, 1 to 2 dr.	...	278	Monel Metal	...	166
" Hexaminæ, Nos. 1 & 2,			Monkey Serum	...	585
1 dr. each	...	450	Monilia <i>var.</i> 503; balcanica	...	379
" Hyd. Biniodidi, <i>var.</i>	...	464	Monochlorbenzene	...	310
" " Perchlor., 1 dr.	...	469	Monochlorphenol	...	21
" " Co., $\frac{1}{2}$ oz.	...	469	Monsel's Salt, $\frac{1}{2}$ to 2 gr.	...	421
" Hydrarsan, $\frac{1}{2}$ oz.	...	183	" Sol., 3-6 m.	...	421
" Hydrastis Co., 1 oz.	...	492	Monsol and Preps.	...	33, 34
" " et. Ergot, 1 oz.	...	492	Monsonia, <i>var.</i>	...	871
" Ichthosulphol, 1 to 3 dr.	...	504	Moodooga Oil	...	845
" Iodi Co., 1 dr.	...	513	Moogrol	...	609
" Ixoræ, 1 oz. inc.	...	864	Moonlight	...	321
" Langdon Brown's, 1 oz.,	1053		Moorhof's Paste	...	509
" Mag. Suph. Co. (Mist.			Morbilli, 996; Mori Succus	...	871
Alba), $\frac{1}{2}$ to 2 oz.	...	548	Morison's B.I.P.P.	...	234
" Malarial, Anti-, 1 oz.	...	747	Moro's Tuberculin Test.	...	947
" Morph. et Phenazon Co.,			Morphina, 1-10 to $\frac{1}{4}$ gr. 558 & 137, 232		
1 oz.	...	563	" Steriloids	...	134
" Moschi, 1 oz.	...	871	<i>Morphinæ Acetas</i> , 561; Diace-		
" Mucilag.	...	795	tyl. and HCl., 1/24 to 1/12		
" <i>Olei Ricini</i> , 1 to 2 oz.	...	—	gr., (and Base), 566; HBr.,		
" Olei Santali, 1 oz.	...	623	HCl., 562; Meconas, 564;		
" Oleo-balsamica, 1 to 4 dr.	...	811	Periodid., 1/16 to $\frac{1}{4}$ gr., 135,		
" Paraldehydi, 1-2 oz.	...	126	564; Sulphas, 564; Hypo-		
" Paral. et Pot. Iod., 1 dr.	...	126	phosphis, $\frac{1}{2}$ to $\frac{1}{2}$ gr., 563;		
" "Patent" et Camph	...	109	<i>Tartras</i> , 1/8 to $\frac{1}{2}$ gr., 565;		
" Plinazon. Expect., 1 to 2			Oleatum (1 to 60)	...	561
dr.	...	329	Morphinæ Methyl Brom., hyp.,		
" Pot. Brom. et Digitalis,			$\frac{1}{2}$ - $\frac{1}{4}$ gr.	...	567
$\frac{1}{2}$ to 1 oz.	...	711	Morphinæ Methyl Chlorid.	...	567
" Pot. Iod. c. Lob., $\frac{1}{2}$ oz.	...	788	Morphine Addicts, 1926, Com.		
" Quininæ Ammon., $\frac{1}{2}$ to 1			Report	...	1014
oz.	...	739	" Habit	...	560
" Quininæ c. Ferro., $\frac{1}{2}$ oz. <i>t.d.</i>	...	728	<i>See also</i> Opium	...	628
" " Co., $\frac{1}{2}$ oz.	...	739	" Emetine in	...	561
" " Eff.	...	738	" Gold in	...	371, 561
" Roseberry's, 1 oz.	...	738	" Narcotine Meconate,		
" Rubra, <i>q.s.</i>	...	777	$\frac{1}{2}$ to $\frac{1}{2}$ gr.	...	569
" Santali Co., $\frac{1}{2}$ -1 dr.	...	623	" Scopolamine	...	498
" <i>Sennæ</i> Co., 1 to 2 oz.	...	886	Morphosan Hypod., $\frac{1}{2}$ to $\frac{1}{4}$ gr.	...	567
" Simarubæ et Granati	...	887	Morton's Fluid	...	512
" Sinton	...	743	Morvette Cod L. Oil Tablets	...	618
" Sod. Ac. Phos., $\frac{1}{2}$ oz., 777;			Morus Nigra,	...	871
Co., $\frac{1}{2}$ oz.	...	777	Moschus, 5-10 gr.	...	871
" Sodæ cum Opio, 1 oz.	...	629	Mosaic Disease	...	887
" Sodii Iodid, Co., 1 dr.	...	775	Moss Accouchement Sheets,		
" Salicyl, 1 oz.	...	71	Compressed Sheets, Dressings		
" Sp. Vini Gall., B.P. '98, 1-2 oz.			Loose, Gauze-Covered Towels,		
" Strych. Phosph., 1 oz.	...	793	Pillows, Sterilisation	785, 786	
" Theilemani, av. 30 min.	...	383	Mosquitoes and Malaria	748, 749 & 556	
" Tomb's Ess. Oil	...	1046	Plant	...	875
" Tussi Rubra, $\frac{1}{2}$ -2 dr.	...	563	" to ward off	...	556
" Tussis Luff, $\frac{1}{2}$ oz.	...	172	" and Bites and Stings	...	1036
" Valerianæ Co., 1 oz.	...	825	Moss, Iceland, 849; Irish	...	851
" Zinc Ox. (et c. Op.), 1 dr.	...	828	Motenol	...	296

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Mother's Advice	632	"N.C.I."	572
Mothersill's Remedy	632	N.E.M.	591
Motor Spirit ...	659 & 144		N.H.I. Amend. Act, 1928.—		
Moulds cause Asthma...	...	666	B.M.J. i./28,677, 811, 1117.		
" Inhibition of	498	Nabarro on Tick Fever, 585,		
Mountain Ash	887	and Sleeping Sickness, <i>vide</i>		
" Damson	887	Edn. XVIII., p. 565.		
Mouth Washes, 81, 97; Per-			Nagana	587
mang., 553; Peroxide	495	Nagelschmidt's apparatus	313
Mowra	844	Nail Polish	888
Much's Modified Gram. <i>vide</i>			Nainsook	436
Edn. XVIII., p. 540			Naphthalene, 2 to 15 gr. ...	572, 275	
<i>Mucilage Acaciæ, ad lib.</i>	1	Naphthalene, Tetrachlor., 3 to		
" Amyli, 12 gr. to 1 oz.	—	12 gr.	573
" Bismuthi	232	Naphtha Mineral ...	120, 659	
" Cydonii	853	" Solvent, 313; Wood ...	119	
" Gummi Indici	2	Naphthalol, 3 to 8 gr.	572
" Marantæ	814	Naphthol a-, 2 to 5 gr. incr. 571, 6		
" Salep	883	" B-, 3 to 10 gr. ...	570, 6, 275	
" Psyllii	879	" Benzoate	572
" Symphiti	889	Naphthol Bismuth, 10 to 30 gr. ...	237, 232	
" <i>Tragacanthæ</i>	814	Naphthol-Camph. Oxidised ...	571	
" Ulmi, 4 dr.	892	" Charcoal ...	571	
Mucin, 5 to 10 gr. ...	963 & 417		" Phenolphthalein ...	189	
Mucuna Pruriens, 1 to 2 gr. ...	424		" Salicyl	572
Mucus	417	Napkins, Dental ...	439	
Muirapuama	871	Naranja, F.E.=Aurantii Amaræ		
Mulberry Juice	871	Cortex		
Mullein, Great	893	Narceina, $\frac{1}{4}$ to 1 gr. & HCl....	872	
Muller's Fluid, 616; Trypsin Test	143		Narcophin ...	569	
Mulls, Adepsine, Anserine ...	570		Narcotic Drugs Combinations	568	
Thiosinamin	765	Narcotina, 1 to 3 gr. ...	573	
Mumps	996	" HCl., 1 to 3 gr. ...	573	
Murexide ...	219, 389		Narcyl, 1 gr. <i>p.d.</i> , 872; Nargentol	281	
Murray on Goitre	714	Nargol ...	281	
" on Thyroid ...	985, 992		Nasal Douches <i>v.</i> Collunaria...	—	
Muscarine ...	5, 837		" Bougies ...	244	
Musgrave Medium	618	" Inhalers ...	556	
Mushroom Poisoning. <i>See</i> Fungi	1103		" Oil ...	467	
Musk (and artif.) ...	316, 871, 61		Nasgar Medium <i>v.</i> Abel and		
" Root	889	Gordon's Bacteriology		
Muskatbalsam	872	Nasturtium ...	872, 166	
Muslin, 436; Mustard ...	763, 160		National Benzol Mixture ...	144	
Mustard Gas ...	1102, 500		National Insurance in D.D.A.		
Musterole	764	<i>See</i> D.D.A.		
Muthanol	243	Nativelle's Digitaline Granules,		
" Suppos.	243	$\frac{500}{1000}$ and $\frac{1}{240}$ gr. ...	399	
Muthu's Inhalants	128	" " Solution, 1 Cc. ...	399	
Mutton Bird Oil, 619; Essences	582		Natrium, <i>see</i> Sodii	
Mydriasine	216	Natto ...	887	
Myelin	959	Nauheim Baths, 257; Salts ...	779	
Mylabris <i>sp.</i>	268	" " CO ₂ in air ...	502	
Myrica Acris, 118; Myrica Gale	844		Neatsfoot Oil ...	37	
Myricin, 2 to 5 gr.	871	Nebulæ ...	574	
Myristica; Myristicin... ..	871		Nebula Acid Boric ...	574	
Myrobalanum, $\frac{1}{2}$ to 1 dr. ...	855		" Acid Lactic ...	55	
Myrosin ...	76, 160		" Acid Tannic T.H. ...	574	
Myroxylon Pereira ...	843		" Alkalina ...	574, 772	
" Toluif. ...	843		" Aluminis, 5 to 15 gr. to oz.		
Myrrh, 5 to 15 gr. ...	872		" Analgesic ...	574	
Myrtillin ...	872		" Antiasthmatica ...	574	
Myrtillus, 872; Myrtol 5 to 15 m.	872		<i>See also</i> Comp. Asthma Fluid		
Myrtus Chekan ...	850		" Antipyridi ...	574	
Myxoedema, Thyroid in, 985, 987			" Antiseptic ...	574	
and Therap. Ind.					

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Nebula Astringent; Catarrh ...		574	Neurasthenia, Gold in ...		371
„ Chlorbutol Co. ...		575	Neurinase, 1 to 4 dr. ...		820
„ Cocainæ HCl. ...		338	Neurine ...		5
„ Cocainæ Co. ...		574	Neutral Red. ...	275, 419, 437	
„ Cocainæ Oleosa ...		335	„ „ Egg Medium ...	927, 618	
„ Creosoti Co. ...		575	Neutralisation Table ...	Vol. I. xxxi	
„ Cupri Sulph. ...		574	New Skin ...	360, 633	
„ Diphtheria. ...		574	“ New Zealand Cream ” ...	598	
„ Eucain HCl. ...		344	Niccolum and Salts ...		166
„ Eucalypti, 574; Co. ...		615	Nickel, 166; Albumose Test ...		364
„ Ext. Supra-renal ...	575, 976		„ Carbonyl ...		501
„ Ferri Perchlor. ...		413	Nicholson's Blue. ...		2
„ Formaldehyd. Muthu ...		128	Nicotiana Tabacum ...		166
„ Hay Fever. ...		575	Nicotina, 1/6 to 1 gr. ...	873, 232	
„ Hydrarg. Nit. ...		467	„ Salicylas, 875; Tart ...	275	
„ Iodi Co. ...		575	Night-blooming Cereus ...		849
„ Lobeliæ Co. ...		574	Night Blue ...	325 & 605	
„ Menthol (Co., 575) ...		557	Nightshade, Deadly ...		222
„ Mucin ...		963	„ Black, Woody... ...		887
„ Phthisis, 575; Pini Co. ...			Nigrosin... ...		535
„ (et c. Cocaine)... ...	575		Nikalgin, 5 to 15 gr. ...		731
„ Potass. Chlor. c. Ferro ...		575	Nikkei Bark ...		298
„ Potassii Permang. ...		574	Nile Blue ...		323
„ Quininae ...		575	Nim ...		842
„ Resorcini ...	574, 752		Nipagin ...	9, 500	
„ Sodii Bicarb. ...		772	Nisbet's Specific ...		623
„ Sodii Salicyl, 20 gr. to oz. ...			Nissl's Stain ...		549
„ Aq. ...			Niton ...		335
„ Stimulant ...		575	Nitre, 716; Nitrated Papers... ...	717	
„ Suprarenal. ...	575, 976		Nitrifying Bacteria ...		615
„ Tonic ...		575	Nitrite of { 1-1 m. by mouth } ...		
„ Zinei Chlor. vel Sulph., 10 ...			„ Amyl { 2-5 m. inhaled } ...	152	
„ to 25 gr. in oz.... ...	574		„ Sterules ...		153
„ Zn. Sulphocarb., 5 gr. to oz. ...			Nitrobacterin ...		615
See also Vapores.			Nitrobutyl-toluene ...		61
Necator var. ...		504	Nitrobenzol ...	310 & 234	
Nectandrine ...		844	Nitro-celluloses ...	359, 440	
Neelsen's Sol. ...		598	Nitro-erythrite, ½ to 1 gr. ...	408	
Neem, Nim ...		842	Nitrogen... ...	636	
Neisser's Bougies, 177; Stains ...		535	„ Active ...	636	
Neisser-Siebert Ungt. ...		471	„ Estn. in Urine ...	381	
Neoarsaminol ...	204, 40		„ Peroxide ...	1102 & 113	
Neo-arsenphenolamine. ...	204, 40		Nitroglycerin, 1-200 to 1-50 gr. ...		
Neocaine ...		69	„ incr. ...	575, 93	
Neocinchophen ...		319	„ Solution, ½-2 m incr. ...	576, 93	
Neokharsivan ...		204	„ Tablets, 1-600, 1-400, ...		
Neolyse ...		546	1-200, 1-100, 1-75, 1-50 ...		
Neon ...		337	& 1-25 gr., also ½ and 1 ...		
Neopelline ...		20	mgr. 577 et seq., 93 (See ...		
Neophenoquin Tabs., 5 to 15 p.d. ...	319		also Tabellæ).		
Neopine ...		139	Nitro group and Basic Nitro- ...		
Neoprotosil ...		173	gen, effect of... ...	255	
Neo-Trepol ...		242	Nitroguaiacol ...		378
Neo-Salvarsan ...	204, 40		Nitrolim... ...		52
Neo-Silver Salvarsan ...		203	Nitro-mannite, 1 gr. ...		409
Neostam ...		168	Nitron ...		60
Nepenthe, 5 to 20 m. ...		631	Nitropropiol ...		377
Nephritis ...	1077, 384		Nitrosalicyl Test ...		378
Nernst Lamps, 57; Neroli Oil ...	842		Nitro-toluene (o. & p.)... ...	350	
Nesfield's Sterilising Method ...	432		Nitrous Oxide, 146, with ether, ...		
Nessler's Solution ...	419		105; Nitrous Oxide & Oxy- ...		
„ Folin and Denis Modifn. ...	385		gen ...	147	
„ Richmond's Modifn. ...	419		Nizin ...	309	
Nettle, 34; Neuralgic Pills ...	247		Noguchi Serum... ...	620	
Neuralgic Powders, 16 gr. ...	249		Nolf's Method ...	627	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Non-specific Protein Injns. ...		667	Oils. Essential ...	600 & 123 <i>et seq.</i>	
" " in Rheumatoid			" " Antisep. power of...		126
Affns. 675, 915, 951			" Saponification Nos. ...		159
Non-staining Scarlet ...		313	Oiled Calico, Silk, etc. .		271
Nordhausen Acid ...		93	Oiled Silk Dextrinised .		271
Norit, 5 Gm. 3 or 4 times daily		846	Oiled Silk Protective ...		271
Normal Horse Serum ...		973	Oils, Akaloidal ...		621
" Saline Solution ...		767	Ointment Bases, 815; m. pts....		243
Normyl Treatment, Edn. XVIII.,		608	Ointments, Absorption .	87,	457
Nosophen. ...		679	<i>See also</i> Mulls and Unguenta.		
Notification of Diseases ...		996	Olea Essentialia ...	600 &	123
" Tuberculosis ...		934	" Antiseptic power of ...		126
Novarsenobenzol ...		204, 40	" " 'T' & 'S' free...		123
" Injection Methods	204,	205	Olea europæa ...		619
Patents and T.M.'s .		204	Oleanodyne ...		601
Doses ...		204	Oleata, 600; Prep'n. of...	601,	604
Guaiacol-Glucose with ...		205	Oleatum Aconitinæ, 1 in 50 ...		100
in dis. other than Syphilis	206,	207	" <i>Hydrarg.</i> , 5 to 25%	602 <i>et seq.</i>	
Suppos. ...		207	" " c. Morph. ...		602
Novarsenobillon ...	204, 40,	276	" " c. Sulph. ...		602
Novaspirin, 74; Novaspirinoids		74	" Morphinæ, 1 in 60 ...		561
Novarsenol ...		204	" Veratrinæ, 1 in 50 ...		893
Novasurol ...		491	Old English Fever Powder ...		738
1 Cc. intram. c. 120 gr.			Olefiant Gas ...		291
Amm. Chlor. <i>per os</i> .—Sir			Oleogens...		660
J. F. H. Broadbent, L. June			Oleo-res Aspidii, 30 gr. .		422
30/28, 1326.			" Capsici ...		272
Novatophan, 8 grains ...		319	" Copaibæ ...		624
Novocain, 1/5 to 1 gr. 346 & 63,		234	" Cubebæ, 5-30 m. .		353
" -Suprarenin ...		347	" Piperis, av. ½ gr. ...		878
" with Strychnine...		347	Oleosaccari, F. Ital., <i>q.v.</i>		
Nuclein, Nucleol, 15 gr. 280,		234	'Oleum' .		93
Nuf. ...		776	Oleum Abietis ...		701
Nutmeg ...		871	" Acidi Salicylici ...		66
Nutrimenta ...		581 & 94	" Adipis = Lard Oil.		
Nutrient Agar, Broth gelatin ...		617	" <i>Ajowan</i> , ½ to 3 m. ...		809
" Powder, Brand's ...		583	" Allii Essent., ½-1 m. ...	837,	276
<i>Nux Vomica</i> , 1 to 4 gr. 598 & 122			" <i>Amygd.</i> , 151; Sterilised. 152, 31		
Nyctal, 5 to 15 gr. ...		820	" " Ess. (et s. HCN) 151, 31		
Nylander's Reagent ...		377	" " <i>Persicæ</i> ...	151,	31
Nylofanol. ...		317	" <i>Anethi</i> , ½ to 3 m. ...		840
Nyrdahl's Dragees ...		863	" <i>Anisi</i> , ½ to 3 m....		840
Oak Agaric ...		838	" <i>Anseris</i> ...	570,	815
Obermayer's Test ...		381	" <i>Anthemidis</i> , ½-3 m. ...		840
Obesity, 966, ('Girdle'), 990,			" <i>Apii</i> , ½ to 3 m. (Celery) ...		170
and Therap. Ind. ...		1078	" <i>Arachis</i> ...		841
Obiturin <i>See</i> Sod. Fluorescein			" Aseptic (Sterilised) ...		152
Obstetrics, Pituitary in. 968, 971			" <i>Atropinæ</i> .		215
Octo-iodo-phenolphthalein ...		146	" " <i>et</i> Scarlet ...		313
Oculenta ...		215	" <i>Aurantii</i> , 842; with Ether	105	
Ocymum .		809, 875	" " Terpeneless .	842,	46
Oenanthe Crocata ...		875	" <i>Benné</i> ...		876
Oestrin ...		170	" <i>Bergamot</i> ...		132
Ogle's Drops, 1 dr. ...		562	" <i>Betulæ</i> , 5 to 15 m.,		65
Ohms 232; Oil of Amber ...		889	" " <i>Pyrolig.</i> ...		705
Oil Sterilised, 152; of <i>Lemon</i>			" <i>Cadinum</i> ...	704,	149
<i>Grass</i> , 875; of <i>Mirbane</i> , 310;			" " <i>Acetic</i> ...		704
Tar ...		704, 149	" <i>Cajuputi</i> , ½-3 m. ...		845
<i>See also</i> Oleum.			" <i>Camphoræ</i> Essent.		262
Oil of Orange in Anæsthesia ...		105	" <i>Camphorat.</i> ...	262,	263
" <i>Vitriol</i> ...		92	" <i>Cantharidatum</i> ...		269
" <i>Wintergreen</i> ...		72	" <i>Carbolicum</i> ...		16
Oil Ether Anæsthesia ...		107	" <i>Carui</i> , ½ to 3 m. .		847
Oils, Iodine, Nos. of ...		86, 37	" <i>Caryoph.</i> , ½-3 m. .	847, 100,	
				164,	498

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE
Oleum Cassiæ, $\frac{1}{2}$ -3 m.	298
" Cedri var.	848
" Celery, $\frac{1}{2}$ to 3 m.	170
" Chaulmoogræ, 5-10 m.	605
" incr.	609
" " Recent Investiga- tions with...	...	609
" Chenopodii, 3 m. ...	534,	850
" Cinereum	455
" Cinnamomi, $\frac{1}{2}$ to 3 m. ...	298 &	60
" Citri	131
" Citron	132
" Citronellæ	129
" c. Cocaina, 2%	335
" Coccois Nucif ...	91,	815
" Colza	764
" Copaibæ, 5 to 20 m.	624
" Coriandri, $\frac{1}{2}$ -3 m.	852
" Cotton Seed	263
" Crotonis, $\frac{1}{2}$ to 1 m.	875
" " Comp.	875
" Croton Elliott, 1 to 3 m.	875
" " Caps., $\frac{1}{2}$ m., two to 5	875
" Cubebæ, 5 to 20 m.	852
" Cypressi	854
" Dugong	619
" " Elliott," 1 to 3 m.	875
" Erigeron, 5 to 30 m.	856
" Eserinæ	621
" Eucalypt., $\frac{1}{2}$ -3 m. ...	613,	129
" Fagi Pyrolig.	705
" Fœniculi, 5-15 m.	857
" Gaultheriæ, 5 to 15 m.	72
" Gossyp. Sem. ...	263,	135
" Graminis Cit.	875
" Gynocardia, 5 to 60 m.	605
" Hedeomæ...	879
" Helianth	619
" Homatropinæ	216
" " c. Cocaina	216
" Hydnocarpæ ...	605,	611
" Hyd. Biniodidi, 1 Cc.	463
" Hyoscinæ ...	498,	621
" Iodoformi et Creosoti	507
" Jecoris	616
" " c. Iodo	618
" Juniperi, $\frac{1}{2}$ to 3 m.	865
" " "Ligni," 865 Pyro. ...	704	
" Lauri	867
" Lavand., $\frac{1}{2}$ to 3 m.	130
" Lemon Grass ...	875,	126
" Limonis, $\frac{1}{2}$ to 3 m. ...	131 ;	
" Terp. less	131
" Lini., 867 ; Lubricans	16
" Maidis	619
" Majorani	876
" Mastiche	869
" Menthæ Pip., $\frac{1}{2}$ to 3 m. ...	870,	132
" " Viridis, $\frac{1}{2}$ -3 m.	870
" Morrhuæ, 1 to 4 dr. ...	616,	133
" " Vitamin 'A' & 'D' in	593 et seq.,	100
" " Unsats. acids in	134
" " Vitamin preps.	618

NAME.	DOSE.	PAGE
Oleum Mor. Aromat., 1 to 4 dr.	618
" " c. Creosot, 1 to 4 dr.	385
" " Phosphorat, $\frac{1}{2}$ dr.	689
" Myrciæ	118
" Myristicæ, $\frac{1}{2}$ -3 m.	871
" Myrti, 872 ; Neatsfoot	87
" Neroli ...	842 &	46
" Nucis Arachis	841
" " Moschatæ	871
" Olivæ Neutrale	620
" Olivæ (sterilised, 152, 620), $\frac{1}{2}$ to 1 oz. ...	619,	135
" Origan	876
" Palma	815
" Papaveris, $\frac{1}{4}$ to $\frac{1}{2}$ oz., or ad lib.	619
" Patchouli	876
" Peach Kernel	151
" Pennyroyal, 1 to 3 m.	879
" Petitgrain	46
" Persic	151
" Petrolei (& Flav., 655)	655
" Petroselin	169
" Phosphorat., 1 to 5 m.	688
" Picis Rect. ...	704,	149
" Pilocarpinæ	621
" Pimentæ, $\frac{1}{2}$ to 3 m.	877
" Pini Pumil.	701
" Pini Siberic	701
" Ptychotis, 1 to 3 m.	810
" Pulegii, 1 to 3 m. ...	879,	133
" Rhodii	875
" Ricini, 1 to 8 dr.	620
" " Aromat., 1 to 8 dr. ...	621	
" Rosæ ...	876,	166
" Rosmarini, $\frac{1}{2}$ to 3 m.	136
" Rusci Pyrolig.	705
" Rutæ Grav.	883
" Sabinæ, 1 to 4 m.	883
" Santali, 5 to 30 m. ...	622,	136
" Sassafras	884
" Scarlet et Atropinæ	313
" Sesami	876
" Sinapis Ex. & Volat. 764,	161,	276
" Soya ...	619,	888
" Staphisagria	888
" Succini, 1 to 5 m.	889
" Terebinthinæ Rect., 2 to 10 m. as Anthelmintic, 3 to 4 dr. ...	699,	148
" Terebinth Æther	699
" Theobromatis 102, 804 &	...	183
" Tca Seed	135
" Thymi, 3 m. ...	809, 892,	167
" Tigli, 1 m.	875
" Valerianæ, 1 to 5 m.	825
" Veratrinæ	893
" Verbenæ Indic.	875
" Wintergreen	72
Olibanum	699
Olio di Fegato Merluzzo	616
" " Iodato	618
Omam (Ajowan)	810

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Omnopon, $\frac{1}{8}$ to $\frac{1}{4}$ gr. ...		632, 138	Osmotic Pressure ...		28
Omnopon-Atrial ...		632	Osseine ...		42
Omnopon & Scopolamine ...		632	Ostelin ...		618, 10
Onguent Napolitaine ...		456	Otalgan ...		328
Onychomycosis ...		570	Otto of Rose ...		876, 166
Opacin ...		679	Ouabain, 791, 835, 74, 162;		
Opal Blue ...		2	Ourari ...		853
Operation Gloves, <i>see</i> Veed p.			Ovaltine ...		633
Opial, Opialum ...		631	Ovamammoid Capsules ...		964
Ophthalmic Bottle ...		214	Ovarian Gland ...		963
„ Lamels, <i>see</i> Lamels.			„ Hormone ...		964
„ Solvent (Harman) ...		217	Oviol ...		618
Opoidine, $\frac{1}{8}$ gr. <i>per os</i>		632	Ovo-lecithin, Elixir, Emulsion,		
Opium, $\frac{1}{4}$ to 2 gr. ...		625 & 137	Inj., Pills, Powder, Tabs.,		
„ Thebaicum=Opium FR. Cx.			etc. ...		539 <i>et seq.</i>
Opium Concentratum ...		631	Ovules, <i>see</i> List... ..		633
„ Conference, League Nations		627	„ Cupri Oleat ...		602
„ Consumption ...		627	„ Masses, 633; Tropical... ..		633
„ Raw ...		625	Owbridge's Lung Tonic ...		633
„ Abuse of ...		627	Ox Bile, 5 to 15 gr. ...		411
„ Smoking ...		627	Oxidases ...		76
„ Granulatum ...		625	Oxycroceum Plaster ...		849
„ as Dangerous Drug 1005 <i>et seq.</i>			Oxygen, 634, 140; Cylinders,		
Opsonins ...		896, 601	Inhaln. App., 635, 140;		
Optochin Base, 3 to 4 gr. ...		387	'Solid,' 496, 634; Water ...		13
Optochin HCl., 3 to 4 gr. ...		388	Oxygen content of the air ...		140
Optophone ...		800	„ and Alcohol Inhaln.,		
Orange Flower Water ...		46	635; Ether ...		104
„ Juice Vitamins ...		104	„ Injections ...		635
„ "Oil" ...		312	„ Mask ...		635
„ Wine ...		842, 26	Oxyhæmoglobin ...		582
Orargol ...		379	Oxylith ...		496, 634
Orcein and Orcin ...		6, 320	Oxymel Scillæ, $\frac{1}{2}$ to 1 dr. ...		—
Orchic Fluid ...		982	„ Urgineæ, $\frac{1}{2}$ –1 dr. ...		892
Orchidin... ..		982	Oxymethylene ...		131
Orchil. ...		91	Oxyntin, 5 to 15 gr. ...		43
Orchis Masculæ ...		883	Oxy-Quinoline Sulphate ...		316
Ordeal Bark, 409; Beans ...		692	Oxyquinotheine Cachets ...		252
Orders in Council ...		1000	Oxysparteina (HCl. and Sulph.)		
Organic Analysis Chart ...		192	$\frac{1}{2}$ to $1\frac{1}{2}$ gr. ...		784
Organic Chemicals, min. qties. 204,			Oxytocin... ..		966, 169
<i>et seq.</i>			Oxyuris ...		1098, 505
Organotherapy ...		957 & 169	Ozæna Vaccine, 50 to 1,000 mill		923
Organotropic property ...		40, 44	Ozokerit ...		653
Orge ...		506	Ozone ...		634, 276, 433
Oriental Sore ...		552	Ozonic Ether, $\frac{1}{4}$ to 1 dr., 495;		
Origanum Sp., 876, 167; Orizaba			„ Inhalers ...		556
Jalap, 864; Orizabin, 1 to 5 gr.		864	Pæonia ...		876
Ormesukker ...		759	PI & P ...		997
Oro-nasal Inhalations ...		386, 556	Pacolol ...		34
Orphol ...		237	'Packets' Preventive... ..		82
Orpiment ...		190	Pagenstecher's Ointment ...		476
Orris Root ...		864	Pagliari's Soln. ...		139
Orseille ...		91, 92	Paints, Cellulose ...		441
Orthocresol ...		30	„ Luminous ...		333
Orthoform, $1\frac{1}{2}$ –3 gr., HCl. ...		345	Pakes' Disc ...		436
Orthotoluidine, 308; Ortol ...		431	Palladium Chloride ...		425, 501
Oryza Sativa ...		839	„ for Iodine in water ...		425
Osacol Jelly ...		657	„ „ Carbon Monox., etc. 425,		
Osazone... ..		375, 377	501		
Oscodal ...		618	„ Colloid. ...		375
Oscol Colloids ...		369	Pallamine ...		375
Oscol Stibium and others ...		369, 378	Palm Kernel Oil ...		103
Osmium Tetroxid., $1/64$ gr. ...		834	Palmetto, 885; Palmitin ...		455
Osmo-Kaolin, 1 dr. or more ...		143			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Palmyra Fibre	542	Para-monochlor-phenol	21,	1045
Pan	844	Paranephrin	976
Panama Bark	881	Paraphenylenediamine	307
'Panama' Bismuth	528, 537	Parasites to Kill	1081
Pancreas	637, 142	Parasitotropic Compds. 195, 527 & 40		
„ Insulin from	640	Para-thormone Lilly	993
Pancreatic Diastase	637	Parathyroid Gland Desicc., 1/60		
„ Solution, 1-2 dr.	638	„ to 1½ gr.	933, 174
Pancreatinum, 2 to 4 gr.	637, 142	„ Tablets	993
„ Incompatibility Expts.	638, 142	„ Refs. timent	994
„ and Bismuth, 1 to 2 dr.	230	„ Standardisation and Cal- cium	993, 174
Pané and Renzi's Serum	926	Para Toluene Sodium Sulphone		
Panopeptone	664 & 633	Chloramide	51
Panoptic Stain	400	„ Sulphone Chloride	51
Pansy, 10 to 60 gr.	894	Paratyphoid Vaccines, 948;		
Pantopon, ½ to ¾ gr.	632	Bacillus . . .	948 & 509,	606
Pantosept Tabs.	50	Paregoric (Scotch, 631), ½ to 1 dr.	630
Papain, 1 to 8 gr.	424, 651	Pareira, av., 30 gr.	876
<i>Papaver Somniferum</i>	625	Paremetol, 1 to 2 dr.	536
Papav. Capsulæ	625	Park, Stanford, on Morphine		
Papaverine . . .	567 & 139,	234	Habit and Alcoholism . . .	371,	561
„ Periodid, ½ gr.	135, 567	Parkinsonism . . .	1082,	545
„ Hydrochlor., ½ to 3 gr.	567	Paroleine	655
„ Sulphate, ½ to 1½ gr.	568	Parotid Gland	964
Papayotin, 1 to 8 gr.	651	Parrish's Ch. Food, ½-2 dr.	418
Papaw Fruit and Juice	651	Parsley, Garden, 169; Fools, 836; Parsley Piert, 837;		
Paper Bibulous Dental	439	Wild	851
Papoose	848	Pas de Calais Work on Typh.		
Pappenheim's Stain	549	Vaccines, <i>per os</i> . . .	898,	950
Para-acet.-phenetidin, 5 to 15 gr.	326	Pasque Flower	879
Para-amido-Ethyl-Benzoate	350	Passiflora	876
Para-amino-benzoyldiethyl- amino-ethanol, HCl.	346	Pasta Acid. Salicyl.	66
Para-Amidophenol	296	„ Arsamín	190
Paracarmine	401	„ Arsenicalis (& Arsenios)	182
Paracresol	30	„ Bismuthi Beck	233
Para Dichlor Benzene	310	„ Bismuth et Iodof.	234
Paradimethylamidobenzald.	365	„ Carbonis et Zinci...	829
Paraffagar, 1 to 2 dr.	658	„ Coll. Argent	377
„ Caps., 1 or 2	658	„ Iodi...	372
Paraffinum Comp. Liq.	658	„ Flava	477
<i>Paraffin. Dur. (& Sterilised)</i>	653	„ Formalini	132
„ Brominated	519	„ Hydrargyri Cyanidi	460
„ Chlorinatum	53	„ Hyd. Zn. Cy.	462
„ Detection of	144	„ Hyd-Oxycy.	461
„ "No. 7"	654	„ Ichthosulphol et c. Ol.	505
„ „ Modif.	654	„ Tcreb.	513
„ Treatment of Burns	654	„ Iodi et Picis	509
„ Liq.	655, 143	„ Iodoformi Cinnam.	829
„ Amer. and Russ.	53, 655	„ Lassar's	709
„ Iodine in	519	„ Londinensis	762
„ Viscosity of	655, 143	„ Mackintosh	509
„ Chlorinated	53	„ Moorhofi	707
„ with Acriflavine	304	„ Plumbi c. Cupro...	536
<i>Paraffin Molle</i> , 653; Iodine val	144	„ Ravaut	752
Paraform, . . .	131, 234, 276,	556	„ Resorcini, Fort. Mitis, et c. Zinci Oxido...	804
„ Collodion	132	„ Theobromatis	829
„ Snuff	132	„ Unna	709
Paraguay Tea	253	„ Vienna	829
<i>Paraldehydum</i> , 30 to 120 m. 125, 234			„ Zinci c. Anylo	829
„ Caps., 20, 30, 40 m.	126	„ „ Composita	829
„ as Anæsthetic	126	„ „ et Gelatini	587
Paralysis, Triment. of by malaria 1080			Pasteurisers	587

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Pasteurisation of Milk		587, 472	Pelletierina, 2 to 6 gr....		660, 234
(<i>See also Milk.</i>)			Pelletierinæ HBr. Sulph., <i>Tan-</i>		
Pastilles, Asthmatic ...		717	nas (2 to 8 gr.), etc. ...		661
" Guimauve ...		431	Pellidol ...		314
" or Jujubes v. Trochisci			Pellitory... ..		380
Réglisse ...		860	Pelosine ...		844
Pastilli, Glyco-gelatin ...		430	Pencils, Iodoform ...		509
" Acid Boric ...	10,	430	Penicillium ...		498
" Acidi Carbolici, $\frac{1}{2}$ gr. .		18	Pennyroyal ...		879
" Aconiti, 1 m. ...		99	Pentachlorethane ...		293
" Ammon. Brom., 1 gr. .		145	Penta-vaccine ...		949
" Bismuth Carb., 3 gr. c.			Pentasulfure d'Antimoine ...		158
" Morph. Acet., 1/40 gr. .		228	Pentosuria ...		379
" Cascara ...		278	Pentyl Hydride (Pentylene) ...		660
" Cocæ Ext., 2½ gr. ...		332	Peony ...		876
" Cocainæ HCl. $\frac{1}{50}$ gr. c.			Pepo, av. 1 oz. ...		876
Antipyrin, 3 gr. ...		338	Pepper .		878
" Cocainæ HCl., 1/10 gr.			Peps ...		633
(et c. Morphina), ...		338	Pepsalia .		770
Cocain. HCl., $\frac{1}{12}$ gr. c.			Peppermint ...		870
Milk Sugar ...		339	Pepsodent ...		259
" Codeinæ, $\frac{1}{2}$ gr....		356	<i>Pepsin</i> , 5 to 10 gr. 661 <i>et seq.</i> &		144
" Convallariæ ...		852	" Incompat. ...		662, 145
" Formosyl ...		130	" Soluble & Insol. ...		662
" Marsh Mallow .		431	Peptic Index ...		418
" Menthol, $\frac{1}{2}$ gr. .		557	Peptone, 663; Water, etc. ...		619
" Morphinæ, 1/30 gr. ...		562	" Bile Test ...		366
" Pine Terpene Heroin... ..		701	Peptone Immunisation in Asthma		667
" Pyrethri ...		880	" Indications & contra-		
" Ravaut's Paste ...		536	indications ...		667
" Stomachici ...		859	" Technique ...		668
" Stovaine, 1/20 gr. ...		353	Peptone Sterules, Intrav. ...		688
" Tamarind Co. ...		890	" " " Cont. Course		668
" Terebini ...		803	" " " Shading off		668
" Terpheroin Co. ...		701	" " " Intram. ...		669
" Thymol, 1/32 gr. ...		811	" " " Cont.		
" Ulmus Fulv. .		892	" " " Course		669
Patchouli ...		876	" " " 10% 10 Cc.		672
Pates Pectorales ...		870	" Witte ...		669
" Patent " Medicines ...		621	" in Arthritis ...		675
" Patent " Mixture ...		109	" in Epilepsy ...		671
Patentex .		729	" in Vaccine Therapy ...		672
Patents and Trade Marks 1027 <i>et seq.</i>			" <i>Per os.</i> (0.5 Gm. <i>t.d.a.c.</i>)		673
Patents, Conference on Empire		1028	" Nolf's Method ...		672
Patents, Designs and Trade			" Danysz ...		672
Marks (Temp. Rules) Act ...		1028	" References ...		673
Patents and Designs Act (1919)		1028	" Serum (Patient's) ...		669
Patent Blue ...		325	<i>See also</i> A. G. Auld, B.M.J. ii./29, 599.		
Pathone .		34	Peptonised Beef, 639, 664; Beef		
Paullinia Sorbilis ...		861	Essence, 582; Beef Jelly,		
Pausinystalia ...		895	639; Chicken Jelly, 639;		
Pautauberge's Sol, $\frac{1}{2}$ oz. ...		385	Beef and Malt 664; Milk ...		639
Pavimol, $\frac{1}{2}$ to 1 oz. incr. ...		619	Peptonising Powders ...		639
Payne's Reagent ...		387	Peptonoids of Beef ...		664 & 626
<i>Pea Nut Oil</i> ...		841	Peracrina ...		305
Pear Essence ...		33	Perborates ...		12
Pearl Disease = Tuberculosis			Percentage Table ...		Vol. I. xxix
of Serous Membranes of			Perchloride, <i>see</i> Hyd., also Solubes.		
Cattle, <i>see</i> Tuberculin Bovine.			Perchlorethylene ...		293
Pearson's Antiseptic Fluid ...		264	Perenyi's Soln. ...		401
" Arsenic Solution ...		185	Perfumed Formosyls ...		600
Pectins ...		167	Perfumes. Synthetic ...		126
Peenash ...		474	Perhydridase ...		76
Pellagra ...		102, 561	Periodic Table of Elements		xxxvi
Pellanthum and Comps. ...		829	Periodides, Alkaloidal ...		135

FIGURES IN HEAVY TYPE, *e.g.* **100**, REFER TO VOL. II.

NAME.	DOSE.	PAGE.	NAME.	DOSE.	PAGE.
Peritoneal Fluid Exam.	...	413	Petrolatum, 653; Iodi, 519;		
Periwinkle	...	894	Liq.	655
Perles Apiol, 3 m., 1 or 2	...	169	Petrolatum Ac. Boric	...	11
„ Camph, Monobr. 2 gr.	...	265	„ Atropinæ	...	215
„ Carbolæ Ac., 1, 2, gr.	...	18	„ Cocainæ 1 to 10%	...	335
„ Chloroform, 3 m.	...	289	„ Creosoti	...	385
„ Creosote, 1, 3 m.	...	385	„ Iodoformi	...	509
„ Ether, 2 m., 1 to 4	...	109	„ Iodi	...	513
„ „ 2 m., c. Tereb., 3 m.	...		„ Zinc Oxidi	...	828
„ Guaiacol, 1, 2, 3 m.	...	446	Petroleum	...	660
„ Izal, 2 m. (Caps.), et c.	...		Petroleum, Burning 659; Ben-		
„ Ol. Morr., 5 m.	...	33	zine, 309, 659; Cerate, 654;		
„ Phosphorated Oil, 1/100,			Emulsion 1 to 4 dr., 656;		
1/65 & 1/32 gr., 1 or 2	...	689	Ether, 660, 234 ; Insecticide,		
„ Quin. Sulph., 1½ gr.	...	737	659; Jelly 653; <i>Spirit</i>	...	660
„ Tar, 2½ gr.	...	703	Pétrole léger	...	660
Perlsucht. See Tuberculin P.T.			Petroselinum Sativum	...	169
Permanganate. See Pot. Permang.			Pettenkofer's Test	...	366
Permutit	...	443	Petty Method	...	628
Peroxide of Hydrogen	...	493	Petzetakis Reaction	...	605
„ Mouthwashes	...	495	Petty Spurge	...	857
Peroxidase	...	76	Peucedanum	...	840
Peroxides in Ether	...	21	Peumus Boldus...	...	844
Persio, 91 ; Persulphates	...	779	Pexuloid	...	361
Pertussin, 1 to 4 dr.	...	892	Pfeiffer's B.	...	921 & 551
Pertussis	...	956, 1098	Pharaoh's Serpents	...	478
Peru Balsam, 5 to 15 m.	...	843	<i>Pharbitis</i>	...	865
Pessaries, Mass for	...	431	Pharmacist's Qualification	...	997
„ Hollow, 431; (<i>q.v.</i> , for			Pharmacy Act, Poisons Schedule		
List); Rubber	...	271			997, 999
Pessaries with Cacao Butter, 15, 20			Phaseolus	...	877, 506
(<i>flat shape</i>), 30, 60 or			Phellandrene	...	130
120 gr.:—			<i>Phenacetinum</i> , 5 to 15 gr.		
Pessus Acidi Borici, 10 gr.	...	10			326 & 65, 234
„ Lactic 2%	...	729	„ c. Caffein, Eff. 1-2 dr.	...	327
„ Acidi Tannici, 10 gr.	...	95	Phenalgine, 5 to 20 gr.	...	3, 234
„ { Acid Tannic, 10 gr. }			Phenazine Compds.	...	302
„ { Morphine, 1 gr. }			<i>Phenazonum</i> , 5 to 15 gr.	...	327 & 276, 234
„ Atropinæ, 1/20 gr.	...	215	„ Eff., 5, 10, 15 gr. in dr.	...	328
„ Bellad. Ext. 1½ gr.	...	226	„ Salicyl.	...	329, 236
„ Bismuth Oxychlor., 10 gr.	...	232	Phenetidin	...	326
„ Chloral Hydrate, 10 gr.	...		Phenetolcarbamide ¼ gr.	...	755
„ Cocainæ, ½ gr.	...	339	Phenobarbitalum 1½ to 5 gr.	...	822
„ Coninæ, ½ m.	...	382	Phenocain	...	345
„ Formosyl	...	130	Phenocoll HCl., 8 to 15 gr.	...	327, 236
„ Glycerin	...	431	<i>Phenol</i> , 1 to 3 gr.	...	13, 4
„ Glycerin Ac. Boric	...	10	„ Bismuth, 10 to 30 gr.	...	237
„ Ichthosulphol, et c.	...		„ Camphorat.	...	15
„ Resorcin	...	504	„ Iodized, 17; Lotion	...	15
„ Morphinæ, ½, 1 gr., et c.			„ Mercury, ½ to 2 gr.	...	459
„ Bellad. Ext., 2 gr.	...		„ <i>Phthaleinum</i> , 2 to 5 gr.	...	
„ Opii Pulv., 2 and 3 gr.	...				677 & 146, 189, 414
„ Plumbi Iodidi, 5 gr. (et c.			„ Tablets	...	678
Atropina, 1/20 gr.).	...		„ Phthalin	...	21, 236, 412
„ Potassii Bromidi, 10 gr.	...		„ Red	...	678, 63, 189
„ Quin. HCl., 3 to 5 gr.	...	728	„ Sod.-Sulphoricinas	...	621
„ Zinci Ox., 10, 15 gr.	...		„ Sodique	...	17
„ Zinci Sulphocarb., 5 and			„ Sulphonephthalein, 6 mgr.	...	
10 gr.	...				678 & 63, 189, 606
Petechial Fever	...	909	„ Tetrabrom. phthalein	...	
Petit's Liquor	...	399, 436	„ Sod. Sulphon.	...	147
Petitgrain	...	46	„ Tetrachlor. phthalein...	...	147
Petrogell, Petrojel	...	657	Phenolaine	...	354
Petrol, 659 & 144 ; Poisoning			Phenolax, ½ to 8 gr.	...	677
659, 1104			Phenoloids	...	30, 1000

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Phenoloid Tablets	32	Picric Acid Wool, Gauze	63
Phenoquin, 8 to 15 gr....	317, 236		„ „ Solution (Esbach's)	363
„ Tablets, 4 and 8 gr. ...	317		„ „ Brass Paste	391
Phenosalyl	20	Picrocarmine	401
Phenyl-acetamide, 2 to 5 gr....	2		<i>Picrorrhiza</i> , 10 to 60 gr.	877
Phenyl-acetyl-Salicyl, 15 gr. ...	82		Picrotoxinum, 1/100 to 1/25 gr.	877, 236	
„ Alanine	305	Pigment Acidi Picrici et Camph. ...	63	
„ amine	307	„ „ Tannici	429
„ Aspirin	82	„ Antiseptic	17
„ Aspirodine, 5 gr. ...	89, 236		„ Argent Nit. Æther	175
„ -carbonate	815	„ Camphoræ Chloral et Men-	...	
„ dichlor. arsine	36	thol	264
„ -dimethyl-iso-pyrazo-	...		„ Casein	590
lone, 5 to 15 gr. ...	327		„ Chloral Camph. et Co. 282, 283	...	
„ hydrate, 1 to 3 gr. ...	13		„ Chrysarobini, et c. Pyro-	...	
„ group, effect of... ..	254		gallol	295
„ propyl-Acetas ...	889		„ Cocainæ et Hydrarg.	342
„ „ Alcohol ...	888		„ contra Tineam	469
„ -hydrazine ...	1060 & 377		„ Delineans...	175
„ Salicyl, 5 to 15 gr. ...	81		„ Eucalypt. Olei et Ac.	...	
„ Sedasprin, 5 gr. ...	89, 236		Sal.	615
„ serines	171	„ Ferri Perchlor	413
Phenylene-diamine, Meta, 308;	...		„ Guaiacol	446
Para	307	„ Iodi, 514; c. Liq. For-	...	
Phlogetan	281	maldehyd., 513; et	...	
Phloridzin ...	877 & 63, 236, 337		Aconiti	513
Phloroglucin ...	6, 415, 481		„ Iodi et Olei Picis	513
Phosferine	634	„ „ Æthereale	513
Phosgene	816	„ „ Carbol	17
Phosphates in Urine	382	„ Iodoformi, v. Collod	
Phosphatia	383	„ Iodolysin	766
Phosphorated Cod L. Oil, 1 to	...		„ Ipecacuanhæ et Arsenici	...	530
2 dr.	689	„ Liq. Arsen.	530
„ Oil, 1 to 5 m.	688	„ Lœffler	413
„ Suet, 1 in 10	689	„ Mandl	513
Phosphatides	134	„ Menthol	557
Phosphorus, 1/100 to 1/20 gr.	687		„ „ c. Guaiacol	558
„ Pentachloride	690	„ Methyl Aspirodine	87
„ Perles, 1/65 & 1/32 gr. ...	689		„ Salol	82
„ Pills ...	689 et seq.		„ Thymol	811
„ Poisoning... ..	688		Pilene, Imperm. Spongio ...	436, 437	
„ Solutus ...	682		Pilewort and Suppos.	881
Phospho Tungstic Acid ...	204		Piliophen	679
Photographic Developer, 296	...		Pilocarpina ...	694, 90, 236	
Sensitisers	317	Pilocarpinæ HCl., 1/20 to ½ gr.	695	
Phthisis	1083	„ Nitras, 1/20 to ½ gr. 695, 90, 236	...	
Phylacogens	957	„ Phenas	695
Phyllosan	633	„ Salicyl., 1/20 to ½ gr. ...	695	
Physiological effect in compari-	...		Pilocarpine Hair Lotion ...	696, 752	
son with chemical constittn. 251	...		Pilocarpus Jaborandi ...	694 & 90	
Physiological Salt Solution ...	767		PILULÆ	696
„ Standardisation ...	176		Excipients, 696; Gelatin-ctg.	...	
(See also <i>Digitalis</i> , <i>Ergot</i> , <i>Stro-</i>	...		697; Keratin, 697; Pearl	...	
<i>phanthus</i> , etc.).	...		Sugar-ctg., 697; Salol-ctg.,	...	
Physostigma Sem., 1 to 4 gr....	692		82, 697; Stearette Coating	...	
Physostigmina, 1/100 to 1/50 gr.	693, 236		697; Varnishing ...	697	
„ Salicyl, 693; Sulph., 1/60	...		{ Ac. arsenios, 1/50 gr. ... }	...	
to 1/20 gr. ...	693, 236		{ Quin. Sulph., 1 gr. ... }	...	
Phytolaccin, 1 to 5 gr....	877		{ Strych. Sulph., 1/64 gr. ... }	...	
Phytosterol	596	{ Phosphori, 1/50 gr.... }	...	
Pian-bois	552	Acidi Arsen., 1/120 to 1/20 gr.	179	
Pichi	877	Ac. Arsen. et Ferri Redact....	182	
Pickle Preservatives ...	500		Acidi Carbolici, 2 gr....	18	
Picrasmin ...	880		Aconiti Tinct., = 2 m., 1 hourly	98	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Pilulæ :—			Pilulæ :—		
Aconitinæ, 1/600 to 1/200 gr.		99	Cascara Ext., 2 gr.
Addison's ...		398	„ Co., 1 <i>h.s.</i> ...		279
Aloes—4 to 8 gr.	Cathartic Co., U.S. IX. :—		
„ Cascara et Hyos. ...		137	Ext. Col. Co., 2½ gr.; Gam-		
„ et Asafetidæ, 4 to 3 gr			boge, ½ gr.; Hyd. Sub-		
„ et Ferri, 4 to 8 gr. ...		137	chlor., 2 gr.; Jalap Res.,		
„ Nuc. Vom. et Bellad ...		137	¾ gr., approx. in 2 pills		
Aloin, 1/10 and 1 gr.	for av. dose.		
„ Co., 1 <i>a. cib. ult.</i> ...		138	Cerevisæ Ferment <i>vide</i> Fæxin.		
„ Strych. et Bellad. ...		138	Champney, <i>Syn.</i> Pil. Hydrarg.		
Aloin, ½ gr.; Podoph., ½ gr.,			Perchlor. Co. Barts. Mer-		
Ext. Cascara, 1 gr., Ext.			curic Chloride 1/32 gr., Aloes		
Bellad., ½ gr., Oleores.			Extract. Nux Vomica Ex-		
Capsici, ½ gr.	tract, Belladonna Extract ½		
Alterativa S.H. :—			grain each. Used in salpin-		
{ Pil. Hyd., 2 gr. ... }			gitis.—Langford Moore,		
{ Pil. Rhei. Co., 3 gr. ... }			P.J.i./20, 39 ...		
Aluminii Chloridi, 2 gr. ...		141	Chlorure Mercurique Opiacées		470
Antidipsom :—			Cocainæ HCl., 1/5 gr. ...		338
{ Strychnine, 1/60 gr. ... }			Codeinæ Co., ¼ to 2 gr. ...		356
{ Atropine, 1/200 gr. ... }			(<i>Mucilage as Excipient not Syrup</i>		
{ Quin. Sulph., 2 gr. ... }			Colchicinæ, Hyosc. et Nuc.)		
Antimonii Conii et Quin. ...		166	Vom. ...		358
Aperiens = Hyd. Col. Ipec. et			Colocynth. Co., 4 to 8 gr. ...		380
Hyos, “78” U.C.H. ...			„ et Hyos., 4 to 8 gr. ...		381
Argent. Cyanidi, 1/60 gr. ...		173	„ c. Ipecac. Aperient,		
„ Nit., 174; et c. Morph.,			= U.C.H., ‘78’ <i>i.e.</i> —		
½ gr. ...		175	{ Pil. Col. Co., 2 gr. c. Pil. }		
Arsamin, ½ gr. ...		190	{ Hyd. 1½ gr. Pulv. Ipecac. }		
Arsenicalis, 1/120 to 1/20 gr.		179	½ gr. & Ext. Hyoscy. 1 gr. }		
„ et Strych., 1/50 gr. ...		181	Compound Bismuth ...		235
Arsen. Hyd. Iodid ...		183, 463	Coninæ HBr., ½ gr. ...		381
Arsen. Ferri et Hyd. Iod.,			Convallariæ Ext., 2 to 8 gr.		852
1 or 2 ...		463	Creosoti, 1 in 2, 2-6 gr. ...		385
Asafetid. Co., 4 to 8 gr.	Crocq., 175; Cupri Acet., ½ gr.		389
Asiaticæ, 1 or 2 daily ...		181	Damianæ Co., 1 <i>t.d.</i> ...		854
Aspirin et Arsen. ...		76	Digitalis Fol., ½ gr., 1 <i>t.d.</i>		
Atropinæ, 1/200 to 1/60 gr.,			„ Opii et Quin. (Heim's) :—		
1 <i>h.s.</i> ...		215	Digitalis, ½ gr., Ipecac.,		
„ Arsen., et Quin ...		215	½ gr.; Opii, ½ gr.; Quin.		
Baillie... ...		398	Sulph., 1 gr. ...		
Belladonnæ, Nucis Vom. et			„ Co St. G.H. ...		393
Cannabis Ext., ½ gr. each		225	Digitoxin, 1/250 gr. ...		399
Beta-Naphthol, 3, 5 gr. ...		571	Diureticæ S.H. :—		
Bismutho-Sodii Sal. cum Salol		235	{ Pil. Hydrarg. Pulv } <i>a.a.</i>		
Blaud's Ferrug, 5 to 15 gr. ...		412	{ Scillæ Pulv. Digital. } 1 gr.		
Blue, 4 to 8 gr. ...		456	Donovani ...		183, 463
Butyl Chloral, 3 gr. ...		247	Dupuytren ...		470
{ „ Hydr., 3 gr. ... }		247	Easton's (et. c. Arsen., 1/60		
{ Gelsemininæ HCl., 1/200 gr. }			gr.), 2 or 3 daily ...		420
Butyl Chloral 2 gr., Camph.			Elaterii Co. ...		855
1 gr., Ext. Gelsem, ½ gr. ...		247	Emetine Bism. Iodide, 1, 2		
Caffeinæ, 1 to 5 gr. ...		248	and 3 gr., <i>Salol, ctd.</i> ...		532
Caffeinæ Triodidi Comp.,			Ergotini, 1, 2 or 3 gr. ...		405
<i>s.t.d.</i> ...		251	Ergotin, gr. 3; Strychnine		
Calcii Chloridi, 5 gr. ...		253	Sulph., gr. 1/64; Ext. Can-		
„ Permang., ½ to 2 gr. ...		555, 769	nab. Ind., gr. ½ (Owen		
Calc. Sulph., 1/12 to 1 gr. ...		261	Lanckester). ...		
Camphoræ ...		264	Euonymin, 2 gr. ...		410
„ Monobrom., 3 gr ...		265	Euonymi Co., Bart's. :—		
„ Salicyl., 1 to 5 gr. ...		265	Ext. Euonymi, 1 gr.;		
Cannabin Tannate 2, 3,			Ext. Aloes, 1½ gr.; Ipecac.,		
4 gr. ...		267	½ gr.; Ext. Hyoscy 1 gr.		
Capsici Co. ...		272	Exalgia, ½ to 2 gr. ...		3

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Pilulæ :—			Pilulæ :—		
Ext. Bellad., $\frac{1}{2}$ gr., $\frac{1}{2}$ gr., $\frac{1}{2}$ gr.			Hyd. Iod. Rub., $\frac{1}{2}$ gr., et Pot.		
Extr. Cannab Ind., $\frac{1}{4}$ to 1 gr.	267		Iod., 4 gr.	464	
Ext. Filicis, 3 m.	422		Hyd. Iod., Vir. $\frac{1}{2}$ to $\frac{1}{2}$ gr.	465	
Ext. Hyoscy., 1 gr., Ipecac., $\frac{1}{2}$ gr.			Hyd. Iod. Vir., B.S.H.—Hyd.		
Ext. Kava, 3 gr.	865		Iod., $\frac{1}{2}$ gr., Opium $\frac{1}{2}$ gr.,		
Ext. Nucis V., $\frac{1}{4}$ gr., $\frac{1}{4}$ gr.,			Ext. Gent., 2 gr.		
$\frac{1}{2}$ gr., Salol, 2 or 3 gr.			Hyd. Perchlor., 1/40 to 1/12		
Fæxin Ext., 3 gr.	280		gr.	469	
Ferri Arsen. (et c. Strych.			„ „ Co., <i>see</i> Pil. Champney		
HCl., gr. 1/60)	182		„ Subchlor., $\frac{1}{2}$ to 3 gr.		
„ (Blaud), Carb., 5 to 15 gr.	412,		Hyd. Subchlor. Co., 4 to 8 gr.		
	79		{ Hyd. Subchlor., 2 gr. }		
„ Carb. Sacch., 4 gr.	—		{ Coloc. Pil., 2 gr. }		
„ Glyceroph., 1 c.cib.			{ Pil. Rhei Co., 2 gr. }		
„ Hypoph. c. Strych. 2			(Army Pill No. 9.)		
or 3 p.d.	691		{ Hyd. Subchlor., 1, 2 gr. }		
„ Iodidi, 3 to 8 gr.	417		{ Pil. Col. c. Hyos., 3, 4 gr. }		
„ Iod. et Sod Arsen	417		{ Hyd. Subchlor., 1, 2 gr. }		
„ Quin. et Strych. Phosph.			{ Opii Pulv., $\frac{1}{4}$ gr., 1 gr. }		
(et c. Arsen.)	420		Hyd. Subchlor., Rhei, Cas-		
„ Sulph. Exs., 3, 5 gr.	420		cara et Capsic.	475	
„ Redact, 1, 2 gr.	411		Hyd. Tannat., 1 to 2 gr.	476	
„ Redacti, 1 gr., Ext.			Hydrastin, $\frac{3}{4}$ & 1 gr., 1 p.d.	492	
Nux. Vom., $\frac{1}{4}$ or $\frac{1}{2}$ gr.			Hyoscine HBr., 1/400 to		
Ferri Sulph., 1 gr., c. Strych.,			1/150 gr.	498	
1/30 gr.			Hyoscyaminæ, 1/200 gr. incr.	503	
Filicis Ext., 3 m.	422		Ichthosulphol Ammon., 2½ gr.		
Galbani Co. (B.P. '98), 4 to 8 gr.			Lith. & Soda (of either		
Garrodii	417		1½ gr.), 4 to 12 daily	504	
Glycerophosphatum, 4 gr.	37		Iodoformi, $\frac{1}{2}$ to 3 gr.		
Gossypii Co., 3 or 4 daily	443		Ipec. c. Scilla, 4 to 8 gr.		
Gout—			Ipecac. c. Uriginea, 4 to 8 gr.		
Pil. Hydrarg. gr., 1; Ext.			Ipecac. (Salol ctd.)	524	
Colchici, gr., $\frac{1}{4}$; Pil.			Iridin, 2 gr., 1 h.s.	864	
Col. c. Hyos. gr. 1½.			Laxativæ Co.	139	
Gregory = Col. Co.	381		Lecithin, 1½ and 3 gr.	540	
Guaiacol, 1 to 3 gr.	446		„ c. Ferri Iodid.	541	
Guy's	398		Lithii Guaiacatis, 5 gr.	543	
Hamilton	381		Male Fern Ext., 3 m.	422	
Hædemaker	76		Meglin	502	
Hutchinson, N.H.W. = Hyd.			Mentholis	558	
c. Cret., Pulv. Ipec. Co.,			Meth. Blue, $\frac{1}{2}$, 1, 2 gr.	325	
a.a. gr. 1.			Monckton	182	
Hydrargyri, 4 to 8 gr.	456		Morphinæ Mec., HCl., Sulph.,		
Hyd. et Digital. Co.	398		$\frac{1}{4}$ gr.	564 et seq.	
{ Pil. Hyd., 2½ gr. }			Naphthol-B., 3-5 gr.	571	
{ Pil. Coloc. Co., 2½ gr. }			Naphthalini, 3 gr.	572	
{ Pil. Hyd., 2½ gr. }			Neuralgic	247	
{ Pil. Rhei Co., 2½ gr. }			Niemeyer	398	
{ Pil. Hyd., 1 gr. }			Opii Pulv., $\frac{1}{2}$ and 1 gr.		
{ Pil. Col. c. Hyos., 4 gr. }		{ 'Third	Papain Co., 1 c. cib.	652	
{ Pil. Hyd., 1½ gr. }		night' }	{ Pepsin, gr. 1, Quin. Sulph. }		
{ Ext. Col. Co., 2 gr. }			{ gr. 1, Strych. 1/30 gr., Ext. }		
{ Ipecac., $\frac{1}{2}$ gr. }			{ Tarax. gr. 2, Gowers		
{ Ext. Hyos., 1 gr. }			Phosphori (Martindale), 1/100,		
{ Pil. Hyd., 3 gr. }			1/50 & 1/30 gr., 1 p.c.	689	
{ Opii Pulv., $\frac{1}{4}$ gr. }			„ c. Ferro et c. Nuc. Vom.	689	
Hyd. c. Creta, $\frac{1}{2}$, $\frac{1}{2}$ gr.			„ „ Ferro, Quin. et		
{ Hyd. c. Creta, 1, 2, $\frac{1}{2}$ gr. }			Strych.	689	
{ P. Ipec. Co., 1, 2, 3 gr. }			„ c. Quin.	689	
Hyd. Oxy. Cyanidi, 1/10 gr.	460		„ c. Strych. et c. Ferro...	690	
Hyd. Iod. Flavi, $\frac{1}{2}$ gr.	465		Picis Liq., 1 to 5 gr., 1 or 2...	704	
Hyd. Iod. Rub., 1/50 to			Picrotoxin, 1/100 to 1/30 gr. h.s.	877	
$\frac{1}{2}$ gr.	462		„ Atrop. et Agaricin	877	

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Pilulæ:—			Pink Pills, 634; Pink Root,		
<i>Plumbic. Opio</i> , 2-4 gr. (about			Indian		888
12½% Opium)			Pinta		562
Plummer's, 4 to 8 gr. (Hyd.			<i>Pinus Canadensis</i> , 878; <i>Pumilio</i> ,		
Sub. Co.)			701; <i>Siberica</i> , 701; <i>Strobus</i> ,		
<i>Podophyllin</i> , 1/30 to 1 gr. ...		708	878; <i>Sylvestris</i>		699
„ Co., 1 or 2 h.s.		708	<i>Piper Betle</i>		844
„ et <i>Quin. c.cib.</i>		708	<i>Piper Cubebæ</i>		852
Poore		708	<i>Piper Long</i> , and <i>Nig.</i>		878
<i>Potassii Bichrom.</i> , 1/10 gr. ...		709	<i>Piper Methystic</i>		865
„ Iod., 1 gr., or more		716	<i>Piperazin</i> , 4 to 10 gr.; Tabs.,		
„ <i>Permang.</i> , 1 to 5 gr.		555	5 gr., 702, 236; <i>Benz.</i> , 236;		
<i>Potentin Co.</i>		871	<i>Glyceroph.</i> ; <i>Salicyl.</i> 2 to 5 gr.		703
<i>Quin. c. Bellad.</i>		225	<i>Piperidine & Acid Tart.</i> , 15 gr.		703,
<i>Quin. Hydrargyri et Opii</i>		737	238		
„ <i>Ipecac. et Camphora</i>		737	<i>Piperin</i> , 1 to 10 gr.		878
„ <i>Salicyl.</i> , 2-6 gr.		734	<i>Piperonal</i>		861
„ <i>Sulph.</i> , 1 to 5 gr.		737	<i>Piroplasmosis</i>		191
„ <i>Valer.</i> 1 gr., (and Co.)		741	<i>Pisani's Test</i>		66
<i>Rhei Co.</i> , 2½, 3, 4 and 5 gr. ...		881	<i>Piscidia</i> , 878; <i>Pistoia Powders</i>		878
{ <i>Pil. Rhei Co.</i> , 4 gr.	t.d.		<i>Pistachia Lentiscus</i>		869
{ <i>Ext. Nuc. Vom.</i> , ¼ gr.			<i>Pistany Mud Baths</i>		1088
{ <i>Pil. Rhei Co.</i> , 2½ gr.	h.s.		<i>Pitch, Burgundy</i>		704
{ <i>Ext. Tarax.</i> , 2½ gr.			<i>Pitchblende</i>		323, 355
<i>Rufi = Pil. Aloes et Myrrh</i> ...			<i>Pitfield's Stains</i>		605
<i>Salol</i> , 2½ gr.		81	<i>Pitibulin</i>		969
<i>Santonin</i> ½ gr.		760	<i>Pitocin</i>		169
<i>Saponis Co.</i> (20% Opium),			<i>Pitressin</i>		169
2 to 4 gr.			<i>Pituglandol</i>		969
<i>Scammon. Co.</i> (B.P.'98),			<i>Pituitarium U.S.</i> ½ gr. ...		967
4-8 gr.			Pituitary Gland		965 & 169
<i>Scillæ Co.</i> , 4 to 8 gr.		885	<i>Anatomy and Physiology</i> ...		965
<i>Sodii Arsenat.</i> , ⅓, 1/64 gr. ...		184	<i>Assay</i>		969
„ <i>Cacodyl.</i> , ½ gr.		187	<i>Contraindication to use of</i>		970
„ <i>Chaulmoograte</i> 'A,'			with <i>Insulin</i>		647, 972
1, 2 & 3 gr.		607	<i>Deterioration</i>		970
„ <i>Oleatis</i> , 2 and 4 gr.		761	<i>Dry Entire</i> 1 to 3 gr. t.d. ...		967
<i>Sparteïn, Sulph.</i> , ¼ gr.		784	„ <i>Anterior Lobe</i> , 1 to 4 gr.		967
<i>Spender, E.G.A. — Ferri.</i>			„ <i>Posterior Lobe</i> , 1 to 4		
<i>Sulph.</i> , 2 gr., <i>Aloes</i> 1 gr.,			gr.		967
<i>Ext. Bellad.</i> , ½ gr.			<i>Galactagogue Action</i>		971
<i>Strych.</i> 1/100 to 1/25 gr.		792	<i>In labour</i> , 968, 971; small doses		169
<i>Sulphatum</i>		261	<i>International Standard</i> ...		169
“Third Night” { <i>Pil. Hyd.</i> , 1 gr. }			<i>Liquid Ext. Entire Gl. Special</i> ,		
{ and <i>Col. c.</i>			½ to 1 Cc. <i>intram.</i>		968
{ <i>Hyos.</i> , 4 gr.			<i>Liq. Anter. Lobe.</i> 1 & 2 Cc.		968
<i>Triplex</i> , 1 to 3		137	<i>Liq. Ext. Infundib.</i> , ½ to 1 Cc.		
<i>Trium Phosphatum</i>		420	<i>intram.</i>		968
<i>Unna's Chaulmoograte</i>		609	<i>Obesity treated</i>		990, 1078
<i>Urgineæ Co.</i> , 4-8 gr.		892	<i>Oxytocin</i>		169
<i>Valerian Co. = Trium</i>			<i>Phys. Examn. Author's</i> ...		970
<i>Valerianatum</i>		741	<i>Pitocin, Pitressin</i>		169
<i>Zinci c. Bellad.</i> , 1 or 2		829	<i>Separation into 2 principles</i>		169
„ <i>Phosph.</i> , ⅓ to ½ gr.			<i>Sterules Anterior Lobe</i> 1 and		
1 t.d.		690	2 Cc.		968
<i>Zn. Valer. Co., E.G.A. = Zn.</i>			<i>Sterules Posterior Lobe</i> ½		
<i>Valer.</i> 1½ gr., <i>Asaf.</i> , 2 gr.,			and 2 Cc.		968
<i>Ext. Ballad.</i> , 1/12 gr.			<i>Tablets Entire glds.</i> 1 gr. ...		967
<i>Pimento</i>		877	<i>Therap. Subs. Act.</i>		969
„ <i>Leaf Oil</i>		878	<i>Uses and Refs.</i> 970 et seq.		169
„ <i>Snuff</i>		878	<i>Vasopressin</i>		169
<i>Pine Apple</i> , 840; <i>Essence</i> ...		28	<i>Pituitarin, Pituitrin</i>		969, 169
<i>Pinewood Creosote</i>		384	<i>Pityriasis</i>		562
<i>Pineal body</i>		964	<i>Pityrosporon Malassezii</i> ...		503
<i>Pinenes</i> , 148; <i>Pinheroin</i> , 1 dr.		701	<i>Pix Burgundica</i>		704

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
<i>Pis Carbonis</i>	299	Poisons, Agricultural 178, 997, 1000		
„ <i>Liquida</i> , 2 to 10 gr.	703 &	149	„ and Pharmacy Acts ...	997	
Placenta	175	„ Arsenic Act ...	1001	
Plague	562	„ „ Willcox's,		
„ Serum	563	„ „ B.M.A. Re-		
„ Vaccine	563	„ „ solution ...	997	
Planadalin, 5 to 10 gr.	...	820	„ Commission of Enqy.	997	
Plantago Ovata	864	„ Gases	1101	
Plasma Glucose Agar	543	„ Coloring of ...	1001, 1003	
Plasmochin	750	„ Disinfectants ...	1000	
Plasmodium vivax, etc.	...	553	„ 'Known to Seller'		
Plasmon Preps.	589	„ „ Defined ...	1003	
Plaster Mulls	570	„ „ Mineral Acids ...	1000	
„ of Paris and Bandages	...	260	„ „ Orders in Council ...	1000	
Plasters, Rubber, White Ad-			„ „ Part I., 1923 Amend-		
hesive, 570, 56 <i>v.</i> also	271	„ „ ment <i>re</i> Sale ...	1012	
Plastic Surgery, 361. <i>See</i> also			„ „ Regulations for		
Paraff. Dur.			„ „ Keeping ...	1000	
Plascitiser	442	„ „ Sales to Medical Men	1012	
Platinocyanide	292	„ „ Schedule ...	998	
Platinum and Chloride, 878			„ „ 'Signed Orders' for	1013	
204; Colloidal	375	„ „ Horticultural and		
Pleural Fluid Exam.	413	„ „ Agricultural (<i>e.g.</i> ,		
Pleurisy Root	842	„ „ Acid. Arsenios, Ac.		
Plimmer's Stain	805	„ „ Carbolio, Ac. Hydro-		
Plombieres Douche	768	„ „ cyanic, Cupri Aceto		
<i>Plumbi Acet.</i> , 1 to 5 gr.	...	705	„ „ Arsenis, Nicotine,		
„ Carb.	707	„ „ Mercuric Chloride)		
„ Guaiacolas	707	„ „ 178, 997, 1000		
„ <i>Iodid.</i> ,	707	„ „ Irish Free State Sched.	1002	
„ Lactas	57	„ „ Labelling of, Order		
„ Nitras	707	„ „ 1924 ...	1002	
„ Oleatum	603	„ „ Northern Ireland		
„ <i>Oxidum</i>	707	„ „ Sched. ...	1003	
Plumbum	705, 149	„ „ Through the post ...	1001	
<i>Plummer's Pill</i> = <i>Pil. Hyd. Sub. Co.</i>			„ „ Wholesale Trading ...	1001	
Pluriglandular Therapy.	...	989	(<i>See</i> also Dangerous Drugs Acts).		
Pneumobacillus & Coccus,	908, 924		„ „ 'Poisonous' Substances	1000	
<i>et seq.</i> & 567			„ „ 'Poke Root' ...	877	
Antibody Soln., Types I., II.,			„ „ Polarimeter ...	157	
III., 50 to 100 Cc.	...	925	„ „ Polenske No. ...	439	
Pneumococci, Types	925, 566		„ „ Politzer Apparatus	289	
Min. Health Rep. ...	923, 926		„ „ Pollacci's Solution	139	
Pneumonia	924, 566		„ „ Pollens ...	665, 919	
„ Optochin in	388	„ „ Pollen Vaccine ...	920 <i>et seq.</i>	
„ Vaccine, 50 m. to 2,000 mill.	924		(<i>See</i> also Protein Therapy.)		
„ and Influenza, 923, and			„ „ Polonium ...	332	
Therap. Index, 1034			„ „ Polygala ...	886	
„ Rockefeller Inst. Work...	925		„ „ Polygonum var. ...	878	
„ Serum, 20 to 30 Cc. ...	925		„ „ Polyneuritis; Polyomyelitis	1085, 567	
„ „ Pane.	926		„ „ Polyporus foment	838	
Pneumothorax, Artificial	...	636	„ „ Polyporus <i>C. officinalis</i>	836	
<i>Podophylli Res. & Indica.</i> , $\frac{1}{4}$ -1 gr.	707		„ „ Polyvalent Sera .	899	
152			„ „ Pomatum Antipsoricum	799	
<i>Podophylli Rhiz.</i>	707, 151		„ „ Pomade Max ...	269	
Podophyllin, $\frac{1}{4}$ to 1 gr. .	707, 151		„ „ Pomegranate Bark ...	660	
Podophyllum Peltatum	707, 868, 151		„ „ Pommade aux Concomb	853	
Podophyllotoxin, 1/10 to $\frac{1}{4}$ gr.	708, 152, 233		„ „ de Lyon ...	477	
Poenia	876	„ „ Reclus. ...	329	
Points, Alum and Copper Sulph.	...		„ „ Ponder's Stain ...	535	
139, 831			„ „ Pond's Tampons.	436	
Poison Bush, 835; Oak, or Ivy	882		„ „ Ponselle's Medium	590, 620	
Poisons, Antidotes to ...	1100		„ „ Poore's Pill ...	708	
(And <i>see</i> Drug in question.)			„ „ Poppy Capsules	625, 139	
			„ „ Poppy, Horned .	859	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Poppy Seed Oil...	...	619	<i>Potass.</i> Salicylas, 5 to 30 gr.	67
Populus, Populin, 1 to 4 gr.	878	„ Silicas	778
Port	26	„ Silver Iodid.	173
Portugeuese Glossary	647	„ Succinas, 5 to 10 gr.	835
Portable Inhaler	556	„ <i>Sulphas</i> , 15 to 45 gr.	717
Portland Cement	144	„ „ and Anæsthetics	353
Post. Vaccinal encephalitis	545	„ „ Acid	718
<i>Potassa Caustica</i>	708	„ Sulphocarb., 10 gr.	717
<i>Potassa Sulphurata</i> , 2-8 gr.	709	„ Sulphocyanid., $\frac{3}{4}$ to 3gr.	718
Potassic Aperient (et c. Pot. Sulphoc.), 1 dr.	717	„ <i>Tart.</i> , $\frac{1}{2}$ to 4 dr.	718
<i>Potass. Acetas</i> , 10-60 gr.	709	„ <i>Tart. Acid</i> , 15 to 60 gr. ...	718, 154	
„ Argent. Iodid	173	„ Telluras	536
„ Arsenis, 1/32 to 1/16 gr.	184	„ et Sodii <i>Tart.</i> , 120-240gr.	782
„ Benzoas, 15-20 gr.	709	„ Tetroxalas	61
„ Biboras.	12	Potassio-Mercuric Iodide ...	463, 419	
„ <i>Bicarb.</i> , 5-20 gr.	709	Potassium ...	708, 152	
„ <i>Bichrom.</i> , 1/10-1/5 gr.	709	Potato, Bacteriological	619
„ Binoxalas	61	„ Starch, 839; in Bread	117
„ Bismuthyl <i>Tart.</i> & Pot.		„ Sweet	864
„ Sod. Bi. <i>Tart.</i>	239	Potentin Pilula Co., 3-6 p.d.	871
„ Bisulph.	718	Potion Gommeuse	1
„ Bitart, 15 to 60 or 240 gr.	718	Potion Iodurée, 3 oz. in dil.	716
„ Boro-tart., 20 to 40 gr.	719	Potter's Asthma Cure	717
„ <i>Bromid.</i> , 5-30 gr. ...	710 & 152, 276		Potter's Walnut Juice Hair Dye	308
„ Cantharidas, 1-400 to 1-200 gr. hypod.	269	Potus Imperialis	718
„ <i>Carb.</i> , 5 to 20 gr.	711	Poudre contre coryza...	557
„ <i>Chloras</i> , 5-15 gr. ...	711, 154, 276		„ d'Ipecacuanha Opiacée, Max. single, 15 grains	525
„ Chlorid.	712	„ de Reglisse Co.	860
„ Chloroplatinite (and ate)	878	„ de Scille	885
„ Chromate	189	„ de Strophanthine au Centième, Max. single $\frac{1}{2}$ gr.	790
„ <i>Citras</i> , 15-60 gr.	712	Powell's Balsam	634
„ „ Eff., 1 dr. ...	—		Prayer Beads	832
„ Cyanidum (1/12- $\frac{1}{4}$ gr.) ...	712 & 154		Precipitate, Black, 458; Red, 477; White	458
„ Dihydric phosph.	718	Précipité Blanc.	473
„ Ferrocyanidum, 8 gr. ...	712, 189, 362		Precipitin.	896
„ Formas, 1-6 to 3 gr.	35	Preface to Vol. II.	iv.
„ Glyceroph., 3-8 gr.	38	Prescriptions, Analysis of D.D.A. ...	1015	
„ Guaiac-sulphon., 15 gr. ...	448, 70		Preservative Solution	19
„ <i>Hydroxidum</i>	708	Preservatives in foods (Benzoic), 2, 492, 493; Salicylic, 13; against moulds	498
„ Hypophos., 1 to 6 gr.	691	(See also Milk, etc.)	...	
„ <i>Iodidum</i> , 5-20 gr.	712	Pressure Sterilisers	259
„ Margosate	842	Prickly Ash	894
„ Metabisulphis	154	Primula obconica	878
„ Nitras, 5 to 20 gr.	716	Procaine... ..	346, 69	
„ Nitris, $\frac{1}{4}$ to 1 $\frac{1}{2}$ gr.	717	Producer Gas	501
„ Osmas	834	Proflavine, 306, 238; Bougies, 306; Patents, 306; Antiseptic Power, 306; Tablets...	306
„ Oleas	601, 760	Prohibition	117
„ Oxalas Acid	61	Proof Spirit ...	114 & 23	
„ Percarbonas	153	„ „ Conversion Factors ...	115	
„ <i>Permang.</i> , 1 to 3 gr. ...	552 & 154, 276		Prophylactic Ointment ...	458, 474, 32	
„ „ Snake B. Lancets	554	Proposote, 10 m.	387, 534
„ <i>Permang. Spray</i> for C. Sp. Fever	912	Proponal, 2 to 8 gr.	820 & 238
„ Persulph.	161	Proprietary Foods, 590; Medicines, 621; Bill	623
„ Phosphas, 1 to 10 gr.	718	'Propyl'	87
„ „ Acid	718	Propyl Alc. Normal	124
„ Picras	63	„ „ Iso	122, 28
„ Pyroborate	12	Propylene	123, 291
„ Quadroxalate	61			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Propyl-piperidine	381	<i>Pulv. Glycyrr Co.</i> , esine Sacch.		860
Prostate Gland	973	„ Gregory, 10 to 60 gr.	...	881
Protargin Mild, 176; Strong...	...	177	„ Guaiaci Co., 20-40 gr.	...	797
Protargen	177	„ Hypoph. Co., 1 to 4 gr.	...	692
Protargol and Sterules of	...	177	„ <i>Ipecac. Co.</i> , 5 to 15 gr.	...	525
„ Jelly	177	„ Jacobi (<i>Antimonial</i>), 3 to		
Protective Colloid	363	6 gr.	...	166
Protein Therapy	664	„ <i>Jalapæ Co.</i> , 10-60 gr.	...	864
„ Non-specific in Arthritis	...	675	„ <i>Kaladance Co.</i> , 10 to 60 gr.	...	865
„ Skin Tests	664	„ <i>Kino Co.</i> , (5% Opium), 5		
„ Shock	673	to 20 gr.	...	—
Protein Test Papers	665	„ Lecithin, 10 to 15 gr.	...	541
Proteins, Food	94, 95	„ Liquiritæ Co., 60 to 120 gr	...	860
Protoactinium	331	„ Lobeliæ Co.	...	717
Protoxalate de Fer, 1 to 5 gr.	...	417	„ Magnes. Boro-Cit. Co.	...	11
Protozoa, <i>see</i> Amœbæ			„ Mag. Hydrox. c. Carb., 1		
<i>Pruni Virginianæ Cortex</i>	878, 154		to 2 dr.	...	546
<i>Prunus var.</i>	151	„ Menthol Cocaine Co.	...	557
Prussic Acid	43	„ Morphinæ Effervescens...	...	563
Pseudoaconitine...	...	20	„ 'Old English' Fever	...	738
Psicain	354	„ Opii, $\frac{1}{2}$ to 2 gr.	...	625
Psoralia	167	„ <i>Opii Co.</i> , 5 to 15 gr.	...	630
Psoriasis...	...	1085	„ Papain Co.	...	652
Psychotria Ipec.	...	523	„ Pectoralis, 60-120 gr.	...	860
Psylli Sem.	...	879	„ Pil. Coloc. Co.	...	380
Pterocarpus	865, 879	„ Potass. Chloratis Co.	...	711
Ptomaines	1104 & 502	„ Pot. Nitritis Co., 43 $\frac{1}{2}$ gr.	...	717
Ptyalin	76	„ Potassii et Sodii Chloridi		
Puerperal Fever Serum	928, 1086		Co., $\frac{1}{2}$ dr.	...	712
Puff Ball	868	„ pro Pedibus	...	142
Pugh's Stain	535	„ Quin. Co., 12 gr....	...	738
Pulegium	879	„ Quin. Arsen. Hydrarg et		
Pulmonary Catarrh Vaccines in	907		<i>Ipec. Co.</i>	...	738
Pulsa, 2 dr.	...	848	„ <i>Rhei Co.</i> , 10-60 gr.	...	881, 157
Pulsatilla, 879; Pulque.	...	879	„ Rosæ Co.	...	876
Pulverette Powder Pills	...	698	„ Salicyl. c. Talco.	...	66
<i>Pulv. A.P.C.</i> , 12 grs.	...	76	„ Santonini Co., 5 gr.	...	760
„ Acetanilid Co., 3 to 5 gr.	...	3	„ <i>Scammonii Co.</i> , 10 to 20 gr.	...	—
„ Aloes c. Canella, 3 to 10 gr.	...	138	„ <i>Sodæ Tart. Eff.</i>	...	782
„ <i>Amygdalæ Co.</i>	...	152	„ Sodii Chloridi Co. (gargle)	...	770
„ <i>Antimonialis</i> , 3-6 gr.	...	166	„ „ Nitritis Co.	...	579, 717
„ Aromat., 15 gr.	...	846, 895	„ Succ. Papav. Cap., $\frac{1}{2}$ to		
„ Aspirin Co., 12 gr.	...	76	2 gr.	...	625
„ Basilicus, 4 to 8 gr.	...	475	„ <i>Tragacanthæ Co.</i> , 10 to 60		
„ Bismuthi Co. (et c. Morph.)	236		gr.	...	814
(Caution! 2 Forms.)			„ Zinci et Amyli	...	829
„ Calc. Chlorinatæ Ac. Boric	48		„ „ Oleat. Co. (p. Pedibus)	...	142
„ Calcii Glycerophosph. c.	37		Pumpkin ...	853, 876, 504	
„ „ Lacte Exsic., $\frac{1}{2}$ oz.	...		<i>Punica Granatum</i>	...	660
„ <i>Catechu Co.</i> , 10-60 gr.	...		Punicine...	...	661
„ <i>Cinnamoni Co.</i> , 10 to 60 gr.	298		Purgatives, 1048 (<i>see also</i> Hyp.		
„ <i>Cretæ Aromat.</i> , 10 to 60 gr.	629		Purgatives).		
„ „ <i>Aromat. c. Opio</i> , 10			Purgen, $\frac{1}{2}$ to 8 gr.	...	677
to 60 gr.	...	629	Purging Agaric	...	836
„ <i>Cretæ Co.</i> (U.S.), av. 30 gr.	383		„ Salt, Tasteless...	...	776
„ Doveri, 5 to 15 gr.	...	525	Purin derivatives...	637, 202, 383	
„ Dyspeptic Co.; Bism.			<i>See also</i> Nutrimenta		
Carb., Sod. Bic., Mag.			Purpuric Fever, Malignant	...	909
Carb. <i>ad. p. æq.</i> , dose 1			Pus in Urine	...	383
drachm...	...		Pussy Willow	...	883
„ Effervescens Co.	...	782	Putty Powder	...	888
„ Elaterin Co., 1 to 4 gr.	...	855	Pyelography	...	297, 298
„ Glyceroph Co., 1 to 2 dr.	40		„ Sodii Iodid.	775, 297, 298	
„ „ cum Lacte, $\frac{1}{2}$ oz.	...	37	Pyoktanin	...	320
„ <i>Glycyrr. Co.</i> , 60 to 120 gr.	860		Pyraloxin	...	64

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE.	NAME.	DOSE.	PAGE.
Pyorrhœa alveolaris (Emetine in, 530), 926; Ionisation for		290	Quinine as Local Anæsthetic ...		731
Pyramidon, 5-8 gr., and Salts, 8-15 gr., 330, 238; Blood Test		412	„ and Black Water Fever...		737
Pyrazolonum-Phenyl-di-methyl-Salicyl.		329	„ Soln. Isotonic		731
Pyrethri Flores and <i>Radix</i> ...		880	„ in Precipitating Labour 108,		748
Pyridine, 5 to 10 m. ... 873, 880, 28			„ in various affections ...		736
„ Carbonic Ac. Diethyl-amide		265	„ Ionisation		238
Pyrocatechin		171	„ opsonised		746
Pyrogallol $\frac{1}{2}$ to 1 $\frac{1}{2}$ gr. ...		64, 6	„ production		725
„ Acetate		64	„ per Rectum		746
„ -Bismuth, 2 to 8 gr. ...		238	„ Synthetic	725,	155
„ Hair Dye		34	„ Tests for	155,	233
„ Oxidatum		64	„ Wound Treatment ...		728
„ Triacet.		65	<i>Quinine in Malaria</i>		743
Pyrogenic Therapy		673	„ absorption and excretion		746
Pyrooleum betulæ, lithanthracis, oxycedri and pini Extractive			„ intramuscular use ...		745
Tar residues, P. Svec. ...			„ „ necrosis from ...		746
Pyrometers		261	„ intravenous use ...		745
Pyromucic Aldehyde		132	„ in England		748
Pyronin		549	„ oral use		743
Pyrosin		399	„ Paramecia Tests ...		257
Pyroxylic Spirit, 30 to 60 m. ...		119	„ pregnancy, during ...		748
<i>Pyroxylin</i>		359	„ prophylactic use ...		747
Pyuria		534	„ rectal injections ...		746
Quackery		622	„ relapses		747
<i>Quassia</i> , Quassin and Suppositories		880	„ standard treatment ...		743
Quaternary Compds		252	„ subcutaneous use ...		746
Quebracho		880	„ toxic effects		749
Queen's Root		888	„ with Calomel		744
Query's Serum		585	„ „ Arsenic		744
Queues de Cerise		560	<i>Quininæ Acetyl-Salicyl.</i> , 1 to 5 gr.		735
Quevenne's Iron		411	„ Aceto-Coumaras, 3 to 5 gr.		28
<i>Quillaria</i>		881	„ Aceto Salicyl. Sulph. ...		735
Quince		853	„ Acid Hydrochlor. 730,		261
Quinetum		724	„ Arsenas, $\frac{1}{2}$ to $\frac{1}{2}$ gr. ...		726
Quinic Acid		726	„ Benzo Sulphon-Amino-phenylarsonas ...		208
Quinidine 719, 720,		156	„ Bisulph., 1 to 10 gr. ...		739
„ in Auricular fibrillation 721,		157	„ Cacodylas, 1 $\frac{1}{2}$ to 4 gr. ...		726
„ Hydrochlor.		722	„ Camphoras, 1 to 10 gr. ...		726
„ „ Acid		722	„ Carbonate		742
„ „ Periodide, 1 $\frac{1}{2}$ to 3 gr. 135,		723	„ Citras, 1 to 5 gr. ...		726
„ Sulph., 5 to 10 gr. 720,		276	„ Di-ethyl-barbiturate ...		820
„ Slipules, 5 and 6 gr. ...		722	„ <i>Di-HCl</i> , 1 to 10 gr. ...		730
„ Sulph. Acid		722	„ Ethylicarb., 3-15 gr. ...		741
Quinina, 1 to 4 gr. (Antimalarial 15 gr.)		725	„ Ferri Citras, 5 to 10 gr. ...		726
„ as Local Anæsthetic ...		731	„ Fluorid., 1-20 to $\frac{1}{2}$ gr. ...		833
Quinine Absorp. & Excretion 746,		155	„ Formas, 'Basic' (subcut. 1 to 3 gr.), 1 to 5 gr. and 'Neutral' ...		727
„ 'Activated' 132, 536, 743			„ Glyceroph., 3 to 8 gr. ...		38
„ Base preps.		732, 156	„ HI and HI. Acid, 1 to 5 gr. ...		732
„ Estimation		155	„ HBr, 1 to 5 gr. ...		727
„ and Bacteria		155	„ „ Acid., $\frac{1}{2}$ to 2 gr. (hyp.)		727
„ Ether and Olive Oil Mixture for Rectal Anæsthesia		108	„ <i>HCl</i> , 1 to 10 gr. ...		728, 276
„ Excretion... ..		155	„ „ Acid., 1 to 10 gr., $\frac{1}{2}$ to 2 gr., hyp. 730,		276
„ Hæmoglobinuria... ..		737	„ „ IntravInj. 4 to 15 gr. 730,		745
„ Hydrogenation		155	„ „ Carbamid., 5 to 15 gr. 731		
			„ „ -Sulph., 1 to 10 gr. 742		
			„ Hypophosph., 1 to 5 gr. 732		
			„ Iodas, 1 to 5 gr. ... 742		
			„ Iodide and Acid 732		
			„ Iodo-Bismuthate 243		

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Quin. Lactas, 1 to 5 gr. ...		732	Radium Emanation Water ...		350
„ Lygosinas, 1 to 3 gr. ...		742	„ Half Value ...		326
„ Mannitol ...	133,	732	„ Heat Evolution ...		335
„ Nasal Douche ...		737	„ Histological changes from ...		339
„ Nucleinas, 1 to 5 gr. ...		734	„ In Atmosphere ...		338
„ Periodid., 1½ to 3 gr. 135,		734	„ Induced Activity ...		336
„ Phosphas., 1 to 6 gr. ...		734	„ Institute Reports ...	346 <i>et seq.</i>	
„ Quinas, 1 to 10 gr. ...		734	„ Katanga Co. ...	323,	326
„ Salicylas, 2 to 6 gr. ...		734	„ Luminous Paints ...	333,	334
„ Sulphas (Acidus, 1 to 10			„ Mache Units ...		336
gr., 739, 276), 735, 233,		276	„ Manufacture ...		322
„ Sulphocarb., 1 to 6 gr. ...		742	„ Mesothorium in ...	325,	334
„ Tannas, 1 to 4 gr. ...		740	„ Mud ...		350
„ Tylmarin, 3 to 5 gr. ...		28	„ Ocular Therapeutics ...		341
„ and Uran. Chlor., 3 to 6 gr. 356			„ Ointment... ...		350
„ Urea, 5 to 15 gr. ...		731	„ Paints ...	333,	334
„ Urethane, ½-3 gr. ...		740	„ 'Period' ...		326
„ Valerianas, 1 to 4 gr. ...		741	„ Properties ...	324 <i>et seq.</i>	
„ for Varicose Veins ...		741	„ Rays, α 332, β 334, γ 334		
Quinoform, 1 to 5 gr. .		727	„ „ Wave Length ...		340
Quinoidine, 2 to 4 gr. .		742	„ Relation c. Uranium ...		326
Quinol, ½ to 5 gr. ...		863	„ Screens ...		349
Quinoline, 316; Blue ...		317	„ Solution ...		325
„ Tartrate. ...		316	„ Sources ...		323
Quinones ...		167	„ Sea Water ...		350
			„ Standard ...		325
Rabies ...		568	„ „ International ...		325
Radiant Heat ...		314	„ Tests for purity ...		325
Radioactive Constant ...		326	„ „ Mesothorium... 325		
„ Elements Table and Notes			„ Therapeutic Use ...		338
on ...	327-330		„ „ after effects ...		346
Radioactivity, Induced ...		336	„ „ Artificial Menopause 344		
Radio Elements, Identity of ...		331	„ „ 'Bomb' Treatment 342		
Radiology ...		291	„ „ Bomb: Free loan.		
„ Erlangen Treatment ...		306	„ „ Ra Comm. 5 Ade-		
(See also X rays).			„ „ phi Terr.—B.M.J.		
Radiomalt ...		549	„ „ ii./29,636.		
Radiomulsin ...		597	„ „ Cross Fire ...		346
Radiostoleum ...		597	„ „ Clinical Index ...		347
Radiostol ...		597	„ „ Containers (Tubes,		
Radio-Synthesis ...		350	„ „ Needles, Plaques, etc.) 348		
Radio-Thorium... ..		325	„ „ in France and Bel-		
RADIUM		322	„ „ gium ...		343
„ Applicators ...		332	„ „ in malignant disease 340		
„ Average Life ...		326	„ „ in non - malignant		
„ Bacteria, action on ...		336	„ „ cases ...		340
„ Bromide ...		324	„ „ M.R.C. Reports ...		347
„ Chemical effects from ...		339	„ „ Menorrhagia ...		344
„ Characters ...		324	„ „ Needle results ...		341
„ Commerce of ...		323	„ „ Screens ...		349
„ Constants ...		326	„ „ Spread Surface ...		345
„ Curie Mme., discovery ...		322	„ „ To replace surgery 342		
„ Detection in the human			„ „ Wax for ...	339,	343
body ...		346	„ Transmutation Table ...		328
„ Disintegration ...	326,	331	„ Yield from Pitchblende... 324		
„ Distance Filtration ...		338	Radix Fraseri ...		845
„ Distribution and excre-			Radon ...		349
tion after giving ...		339	Ragazzoni's Injection ...		463
„ Electrical properties ...		324	Ragweed	665,	886
„ Electroscope ...		334	Ragwort... ..	665,	886
„ Emanation ...	335,	349	Rami Syrup ...		246
„ „ Mache Unit ...		336	Ramsay on Emanation ...		335
„ „ 'Seeds' ...		349	Ranunculus Ficaria ...		881
„ „ Standards ...		336	Rape Oil ...		764
„ „ Therapy ...		348	Rasorite		3

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Rasot	844	Revelliod's Method	235
Raspberry	882, 883	Rhamni Frangulæ Cortex	858
Rat poison, Arsenical	35	<i>Pursh. Cort.</i> , 3 to 15 gr.	276
Rats, Squill, etc., for	885	<i>Rhatany Root</i>	866
Ravaut's Paste	536	<i>Rhei Radix</i> , 15 to 30 gr.	881, 157
Ravogli's Liniment	17	Rheumatism Serum and Vaccine (<i>v.</i> also Therap. Index) 927, 928
Raw's Tuberculin	941	Rheumatoid Arthritis—B. Coli and B. Typh. in, 675, 915, 1088
Rayon	439	Rhigolene	660
Rebipel Agar	437	Rhinoculin	350
Receptors	897	Rhizopus	498
Reclus Pomade	329	Rhodallin	764
Reconstituted Cream	487	Rhodamines, 678; Rhodinol	166
Rectified Spirit	113	Rhotanium	878
Rectal Feeding, <i>see</i> Enemata	402	Rhubarb Leaves, 882; Root	381
Recurrent fever	568	Rhus Aromat., 882; Glabra, 882; Toxicodendron	882
Red Biddie	26	Rice, 839 and Beri-Beri 593, 505, 506
Red Bone Marrow	958	Richardson's Solution	440
Gum, 5 to 20 gr.	856	Richmond's Nessler Reagent	419
Lead	707	Ricinus	620
Neutral (<i>see</i> also Neutral R.)	927 & 437	Rickets, 1088 (<i>see</i> also Accessory Food Factors, 594 & 98 <i>et seq.</i>)
Precipitate	477	Rickets, Light in relation to	596
Root	866	Rickettsia	609
Sanders' Wood	879	Rideal-Walker Coefficient	262
Scarlet	313	of Oils	128
Soudan III.	326	Riegler's Test	360
Water Fever	191	Rimini's Test	370, 481
Redwood Viscometer	143	Ringer's Solution	767
Refrigeration	22, 483	Ringworm, Fungi, 569; Oint- ment, 704; Infective period	996
Regenerative Tablets, 6 <i>p.d.</i>	769	Thallium Acet. for	891
Regional Anæsthesia & Novocain	347	Rivanol	307
Reichard's Test	66	Robert's Test	363, 378
Reinsch's Test	37	<i>Rochelle Salt</i> , 120 to 240 gr.	782
Relapsing Fever 190, 485 & 568	Roche's Embrocation	634
Remijia Species	387	Rodinal	296
Remittent Fever applied to varied malaria types <i>v.</i> 558	Roeder's Gut	542
Bilious	613	Röntgen Rays	291
Renaglandin, Renastypsin	976	Rogers, Sir L., on Dysentery 526, 527, 529
Renal Function Tests	62, 384	Romanowsky's Stain	396
Renner's Lymph	953	Rongalite	204
Rennet, Essence, Tablets	661	Room Disinfection 127, 131, 18, 272
Rennin 589, 637, 661 & 76, 77, 417	Rosa Damascena, 876: <i>Gallica</i> 882
Renninogen	417	Rosalane	461
Rennin Zymogen	417	Rosaniline HCl., $\frac{1}{2}$ to 4 gr.	320
<i>Resina</i>	881	Dyes	2, 598
Carbolica, R.D.H.	18	Rose Bengal	148
Ipomœæ	864	Roseberrys Mist., 1 oz.	738
Jalap, 2 to 5 gr.	864	Roseine and Acetate	320
Resistance, Electric	283	'Rose Oil'	312
<i>Resorcin</i> , 1 to 5 gr. 750, 6, 238, 276	Roseola, Epidemic	996
Blue	91	Rosettol	876
Hair Lotion	751	Rosindol Reaction	437
Hexyl, 2 to 10 gr.	753	Rosolic Acid	129, 413 599
Ichthyol	505	Ross, on Malaria Relapses 743, 745, 747
-monacetate	752	Rothera's Test	21, 359
phthalein Anhydride	678	Rouge, Polishing	93
Test for HCl. and Ligne- fied Tissue	416	Roux's Stain	536
Resorcinol	750	Rubber, India, 270 and 56; Bandages	270
Respiration, Artificial	146			
Respirator Solution	94			
Rest Light	779			
Retinal Extract, 2 dr.	961			
Reudel Bath Saltrates	634			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Rubber, Dental	270	Sal Emsanum, Fact., 781; Hun-		
„ Gloves	270, 261	yadi Janos, Vichy, Wild-		
Rubella	996	ungen	781
Rubia Tinctorum	882	„ Enixum	718
Rubine	320	„ Limonis	61, 238
Rubini's Camphor, 2 to 5 m.	264	„ Marinum Artif.	770
Rubus Chamaemorus, etc.	882	„ Polychrestum, 30 to 120 gr.	718
„ Villosus	883	Salad Oil	263, 619
Rue, 883; <i>see also</i> Harmine	861	Salaspin, 5 to 15 gr.	74
Ruhmkorff Coil...	291	Sale of Food and Drugs Act....	...	491
Rum	26	Salep	883
Rumex Sp., Rumicin, 1 to 4 gr.	883, 167	Saletin, 5 to 15 gr.	74
Rusby H. H. on Cinchona.—			Salicifrice	762
C.D. and P.J., Oct. 5, '29.			<i>Salicinum</i> , 5 to 20 gr.	80, 238
Ruspini's Styptic	634	Salicyl. Piperaz, 2 to 5 gr.	703
Russ. Hemp Seed	845	„ Salicylate, 15 gr.	73, 238
Russian Paraffin Liq.	655	„ Sulphonic Acid	361
Russo's Test	605	Salicylic Cream, 1 in 6½	66
Russolax, 2 to 4 dr.	655	„ Gauze, Lint, Wool	67
Ruta	883	Salicyl Santalol...	623
Rutile	58	Saligenin, 10 gr.	79
Ryutan	859	Salicylosol	67
Sabadilla (Cevadilla)	893	Saline Gelatin	424
Sabal	885	„ Normal	767
Sabina	883	„ Solubes, Sterules	767
Sabouraud's Pastelles, Milk			Saline and Ether	105
Serum...	548	„ Hyper and Hypotonic	768
Sabromin, 15 to 45 gr....	...	523	Salipyrin, 15 to 30 gr....	...	329
Saccharas Ferricus	411	Salit (inunction), ½ to 1 dr.	73
Sacch. Ferric Oxide, 10 to 40 gr.	415	Saliva	77
Sacharated Iron Carb., 10 to			Salix, <i>var.</i> , Nigra Discolor	883
30 gr.	411	Salmonella bacteria	509
<i>Sacch. Iron Posph.</i> , 5 to 10 gr.	415	Salodine	714
Saccharides	94	<i>Salol</i> , 5 to 15 gr., 81, 240 ; c. Cam-		
Saccharin, ½ to 2 gr. 754 & 238 , 277			phora, 82; Catheter Oil, 82;		
„ Tablets...	755	Collodion, 82; Emulsion, 82;		
Saccharomyces Cerevisiæ (<i>see</i>			Mouth Wash, 81; Pill Coat-		
<i>also</i> Yeast)	279	ing	82, 697
Saccharosan	758	Salophen, 10 to 15 gr.	90
Saccharose	755	Saloquinine	240
<i>Saccharum</i> Amylac.	426	Salt, Table, 766; with Pot.		
„ <i>Lactis</i>	866	Chlorid.	712
„ <i>Purificat.</i>	755, 157	„ Iodised	714
„ Saturni, 1 to 5 gr.	705	„ Baths, 770, 779; Salt free		
Sachs-Georgi Reaction..	...	583	„ diets	770, 766
Sacred Bark	276	„ of Sorrel	61
Saffron	852	„ of Tartar 711; of Lemon	...	61
Safranine Test	378 , 505	„ Packs	768
Safrol, 20 to 30 m.	884	„ Anti-Catarrhal, etc.	18
Sagapenum, 883; Sage	883	Salts, Mineral in foods..	...	96
Sahli's Caps	698, 61	Sahufer	778
St. Ignatius Bean	599	Salurene	453
St. Ivel Lactic Milk and Cheese		59	Salvarsan, 0·1 to 0·4 Gm. 194, 39		
„ Jacob's Oil	634	„ Silver, 0·1 Gm.	203
St. John Long's Liniment	700	„ Sodium, 0·3 to 0·45		
Sajodin, 15 gr.	522	Gm.	202
Salacetin	74	Salvarsanised Serum	200
Salacetol, 10 to 30 gr.	80, 238	<i>See also Arsenobenzol.</i>		
Sal Acetos	61	Salve Soap, 870; Salvia	883
„ Alembroth & Injection 472, 274			Sambuci Flores, 883; Sanagen	...	38
„ Ammoniac <i>v.</i> Ammon. Chlor.			Samsonite	575
„ Bromatum Eff., 60 to 120 gr. 771			Sanaphos, 2 dr....	...	38
„ Carolinum, 20 to 60 gr.	780	Sanatogen	38
			<i>Sandal Wood Oil</i> , 5-30 m.	622
			Sandarach Solution	697

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Sander's Wood, Red	879	Scarlatina, Dick Test & Pro-		
Sandoz Felamine	454	phylaxis, 929; Schultz-		
Sanguinarin, $\frac{1}{4}$ to 1 gr.	884	Charlton Reaction 929 & 570		
Sanguis Draconis, 854; Sangui-			„ Serum ...	928, 929	
suga, <i>vide</i> Hirudines	961	Scarlet Colors ...	313, 277	
Sanitary Towels ...	436, 786		„ Non-staining ...	313	
Sanitas and Preps. ...	701, 264		Sceleth's Method ...	628	
Sanmetto	885	Schedule of Poisons ...	998	
Sanodora Moss Sheets	786	Scheele's Green, 1/100 to 1/25 gr. 184		
Sanocrysin	219	Scheibler's Reagent ...	69	
Sanogyl	203	Schereschewsky's Quin. Ung. 729		
Sansiviera	884	Schiassi's Method ...	517	
Santalol, Caps., 5 m. Forma-			Schick Test in diphtheria ...	538	
gules, Tabs., 3 m. 622, 136			Schierling. ...	381	
„ Methyl Salicyl., 4 m. 623, 240			Schiff's Reagent ...	24, 481	
„ Salicyl-ester, 15 to 30 m. 623			Schindler's Jelly ...	177	
Santalum Rub.	879	Schmiedeberg's Rules ...	253	
Santal Oil	622	Schœnocaulon ...	893	
Santheose	805	Schultze's Mixture and Reagent 154		
Santoninum, 1 to 3 gr. 759, 240			Schultz-Charlton Reaction ...	570	
„ Golden, 2 to 5 gr.	760	Scilla, 1 to 3 gr., 885, 167; <i>Indica</i> 892		
Santyl, 15 to 30 m.	623	Sclavo's Anthrax Serum 905, 505		
Sanusia Sempules	236	Sclerosis Disseminated & T.A.B.		
Sapo Anim., Dur., Kalinus			Vaccine ...	951	
Medic., Moll., 760, 761, 158;			„ C.S. Fluid Exam. ...	409	
Moll. peroleat, 761; Venetus,			Scoparii <i>Carumina</i> ; Scoparin... 784		
Virid, 760 <i>et seq.</i> See also			Scopola var. ...	885	
Castile	158	Scopolamine ...	496	
„ Lanolin	100	„ <i>HBr.</i> , 1/200 to 1/100		
„ Ol. Tereb.	701	gr. 498; HCl. & HI. 500		
„ Superadipat.	761	„ Nitrogen Oxide ...	500	
„ Thymol	811	„ Lævo. ...	498	
Sapones	760 & 158	„ Morphine Anæsthe-		
Saponification, Bolton's way			sia, 498; with		
without soap	762	Atropine ...	499	
„ Nos. of Fats	159	„ „ c. Ether Saline ...	106	
Saponins	884	Scotch Paregoric, $\frac{1}{2}$ -1 dr. ...	631	
Sapotoxin	881	Scotch Fir ...	699	
Sappan	861	Scott-Wilson Test ...	21, 360	
Sarcinæ	418	Scott's Dressing .	457	
Sargol	634	„ Emulsion .	634	
Sarkosin...	95	Scurvy (& Therap. Ind.) ...	597	
Sarsæ Radix, Sarsaparilla	884	Scutellaria (Skull-cap)... 385		
Sassafras	884	Sea Holly, 856; Poppy, 859;		
Sassy Bark	409	Salt, Artificial, 770; Tangle,		
Sauce Preservatives	500	866; Water, Artificial, 769;		
Sauerin	57	Water, Iodine in, 428; Radium		
Saurolo	503	in, 350; Treatm., 769; Radio		
Saussurea	164	Activity ...	350	
Savaresse's Capsules	623	Seaweed .	858	
Savory and Moore's Food	590	„ wrack ...	858	
Savin Oil, 1 m., 883; Saw-Pal-			Sealcones ...	478	
metto, $\frac{1}{2}$ to 2 dr.	885	Sealed Tubes of Gelatin 424;		
Sawyer's Ointment	525	Glucose, 427; Saline... 767		
Saxin	754	Secale Cornutum, 15-60 gr. ...	403	
Saxonite...	575	Secondary List of Drugs ...	832	
Scabies Ungt. See also Therap.			Secret Remedies ...	621	
Ind.	799	Secretin Extract ...	961	
Scales' Benedict Test	371	Secretin (and Tabs., 960) 961, 175		
Scammoniac Rad. (Res., 3-8 gr.)			Secretogen Elixir, 1 to 2 dr. 961		
864, 885, 160			Section cutting and Stains ...	616	
Scammonin, 1 to 5 gr. 864, 885			Sedasprin, 5 gr. 84, 240, 277		
Scammonium, 5 to 10 gr. 864, 885			„ Salts ...	85	
Scarlatina and Vaccine 929, 570, 574			„ Liberation of Br. .	85	
„ Infective Period	996	“ Sedell,” 1 to 2 dr. in aq. ...	228	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Sedobrol Tabs., 1 to 3 <i>p.d.</i> ...		771	Sheep Dips ...		178
Segra ...		857	„ Wool, 436; Shellac ...		887
Seidlitz Powder ...		782	Sherry ...		26
Seigel's Syrup ...		635	Shipway Apparatus ...		285
Seignette Salt, 120-240 gr. ...		782	Shircore on Bismuth Arsanilate ...		241
Sel Anglais ...		546	Sidonal, New, 30 gr. ...		703
Sel de Barnit, 96; de Javelle... 45			Sigma Reaction ...		583
Selenium ...		800	Sigmoidoscopy ...		529, 534
„ Colloidal ...		800	Sil-Al., 1 dr. ...		143
„ Comps., Organic ...		168	Silica, 778; Silicon Carbide ...		295
„ Lead in Cancer ...		374, 511, 515, 531	Silicates, Soda and Potash ...		778
„ Oxide ...		800	„ Ionisation ...		288
Self Inflator Drops ...		289	Silicosis ...		778
Seliwanoff's Test ...		379	Silk, Artificial, 439; Sutures ...		542
Sellard's Test ...		361	Silkworm Gut ...		542
Semen Stains and Tests ...		615, 616	Silk, Genuine, Tests for ...		440
Semolina ...		108	Silver Colloidal ...		376
Sempervivum ...		886	„ Gelatose ...		177
Semprolin Emulsion ...		657	„ Hair Dye ...		34
Sempules, 801; Senecio. <i>var.</i> ... 886			„ Ionisation ...		288
<i>Senegæ Radix</i> ...		886, 168	„ Nitrate, $\frac{1}{2}$ to $\frac{1}{2}$ gr. ...		174
<i>Senna</i> (and <i>Pods</i>), 10 to 30 gr. 886, 160			„ Mitigated ...		175
Sensitol Red, etc ...		317	„ „ <i>Toughened</i> ...		175
Sensitised Vaccines ...		901, 956	„ Oxide, $\frac{1}{2}$ to 2 gr. ...		175
Septamid ...		52	„ Protein, Mild, 176; Strong ...		177
Septicæmia Serum ...		928	„ Salvarsan... ...		203
Sera Chapter, 896; Sero-Vaccines 956			Simaruba ...		536, 887
Serpent Venom ...		960, 571	Simpson Light ...		315
<i>Serpentaria Rhizoma</i> ...		886	Sinalbin, Sinigrin, Sinapis ...		763 & 160
Serum Agglutination (B. Coli), 438; Typh. ...		603	Sinclair's Glue ...		863
„ Anti-colon B. ...		914	Singleton's Ointment ...		635
„ Antidiph. & Purif. ...		915, 537	Sirop des cinq. Racines ...		169
„ Anti-Gas-Gangrene <i>See</i> Peritonitis and Toxæmia, Therap. Ind. ...			Sirop d'Erysimum, $\frac{1}{2}$ oz. ...		856
„ Antilytic ...		973	(<i>See also Syrupus</i>).		
„ Antimeningo ...		912	Sistomensine Tabs., 1 or 2 ...		960
„ Anti-pneumo. (Pane, 926) ...		925	Skin Food, 448; Cream ...		814
„ Antitetanic ...		931	„ Reactions ...		664
„ Diphtheria, 8,000 units (Proph. 500 to 1,000)... 915			„ Tests ...		664
„ „ Conc. ...		916	„ Sterilisation, 470; (Mercuri- crome, 480); Iodine, 518; Thymol, 310.		
„ Dysentery ...		917	Skull Cap = Scutellaria... ...		885
„ Ferruginous ...		40	Sky Writing ...		58
„ Flexner's ...		912	Sleeping Sickness ...		1094 & 586
„ Hæmostatic ...		974	(<i>See also Trypanosomiasis</i>).		
„ Horse ...		973	Slippery Elm Bark ...		892
„ Nevrosthénique ...		40	Slipules ...		698
„ Normal Horse ...		973	(<i>See also Individual Drugs</i>).		
„ Peptone in asthma ...		669	Smallpox ...		953, 996
(<i>See also Diseases or Organisms and Vaccines</i>)			„ & chickenpox diagnosis... 953		
Sesquiterpeneless Oils ...		123 <i>et seq.</i>	Smallpox in England ...		954
<i>Sevum Benzoatum</i> ...		689	Smedley's Paste ...		273, 635
„ Phosphoratum ...		689	Smelling Salts, Carbol ...		18
„ Præparatum ...		689	Smilax Sarsaparilla ...		884
Sextol ...		294	Smoke Screens ...		58
Shale ...		656	Smoking, Anti-Gum ...		880
Shavex ...		159	Snake Bite, 960, 1091; Lancets ...		554
Shavg. Brushes & Anthrax ...		906	„ root, 851; Black ...		851
„ Soap ...		159	„ Venom ...		960
Shaw-Mackenzie on Lipase in Cancer and Tuberculosis 761, 763			„ vine ...		857
			„ weed ...		857
			Soamin, $\frac{1}{2}$ to 3 gr. increased ...		189
			Soap Bark ...		881
			„ Liniment ...		762
			„ Solution, Ethereal ...		76

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Soap and Spirit Lotion. ...		762	Sodii Citro-Tart. Eff., 1-2 dr....		
Soaps, Castile, Household, Shav- ing, Medicated, etc., 760 <i>et seq.</i> , 158,		277	" Coumaras Sol., 25 m. ...		27
" Resin and Silica in ...		159	" " c. Novocain, 25 m..		27
" Solution, Standard ...		420	" " et Adrenalin, 35 m.		27
Sobbbrol ...		9	" Desoxycholas ...		784
Soda Caustic ...		774	" Dibrom-oxy-mercury- fluorescein ...		479
" 'Crystal' Conc. ...		772	" Di-iodosalicyl ...		72
" Tartarata, 2 to 4 dr. ...		782	" Dimethylarsinas, $\frac{1}{2}$ to 1 gr.		186
Sodii Acetas, 15 gr. ...		766	" Dioxidum ...		496
" Aceto-coumaras ...		28	" Dioxydiamido-arseno-ben- zene-mono-methane Sulphonate ...		204
" Acetylaminophenylars, $\frac{1}{4}$ gr. ...		191	" Dioxy-diamino-Arseno- benzene dimethylene Sulphonate ...		207
" Acetylaminohyd. phen. ars., $\frac{1}{4}$ gr. ...		192	" et Ammon. Phosph. ...		777
" Acetyl-Am. Stibinate ...		168	" et Mag. Sulph. Eff., 1 dr. or more ...		780
" Acetyl-Arsanilate, $\frac{1}{2}$ gr. ...		191	" et Mag. Sulph. c. Caffeina 1 dr. or more ...		780
" Acetyl-Salicylate, 5 to 15 gr.		79	" et Potass. Tart., 120 to 240 gr. ...		782
" Am.-Phenol arson., $\frac{1}{4}$ to 3 gr. ...		189, 38	" Ethylas (and Liq.) ...		774
" Antim. Thioglycollate ...		169	" Fluorid, 1-20 to $\frac{1}{2}$ gr.		833, 277
" Arsanilas ...		189	" Formaldehyde Sulphite...		204
" " with Mercury & with Arsenic, & with Antim. Tart. ...		190	" Formas, 1-6 to 3 gr. incr.		35
" Arsenis, 1-64 to 1-16 gr. .		181	" Glyceroph., 5-10 gr.		38, 7, 240
" Arsenas, 1-40 to 1-10 gr.		184	" Glyco-cholas, 2-6 gr. ...		782
" Arseno-phenyl-Dimethyl- Aminopyrazalon-Methy- lene Sulphoxylas ...		208	" Gynocardas ...		607
" Benzozas, 5 to 30 gr. ...		8, 498	" Hippuras, 5 to 30 gr. ...		8
" Benz-sulph.-amino- phenylarsonas .		208	" Hydnocarpus, 10 Cc. 1%		611
" Biboras, 5 to 20 gr. ...		12, 3	" Hydrosulphid. ...		94
" Bicarbonas, 5-30 gr. ...		771	" Hydrosulphis. ...		94
" " Sterilisation ...		261	" Hydroxid. ...		774
" Bism. Tart. for Injection		238	" Hydroxyam.-phenylars.		191
" " Acid 2 to 5 gr.		239	" Hydroxy-Mercury Fluores- cein ...		478
" Bisulphas... ...		779	" Hydroxy-Mercury Salicyl. Acet. ...		473
" " Tabs. for baths ...		779	" Hypobrom., Sol....		387
" Bisulphis, 5 to 30 grains		781	" Hypochloris ...		45 <i>et seq.</i>
" Bi-uras ...		390	" Hypophosph., 3-10 gr. ...		691
" Boras ...		12, 3	" Hyposulph., 10-60 gr.		93, 161
" Boro-Salicyl, 5 to 45 gr....		10	" Ichthosulphol ...		504
" " Tart., 20 to 40 gr....		12	" Iodas, $1\frac{1}{2}$ gr. Hyp.		834
" Bromid., 5-30 gr. ...		770	" Iodidum, 5 to 20 gr. ...		774
" Cacodylas, $\frac{1}{2}$ to 1 gr		186, 240	" Indigo Sulphonas ...		62
" Carbolas ...		17	" Iodo-hydroxyquinol Sulph.		319
" Carb. (Exsic., 3 to 10 gr., 772); 5 to 30 gr. ...		772	" Lactas, 5 to 10 gr. ...		67
" " Monohydrat ...		772	" Mag. Sulph. Eff., 60 gr.		780
" Chaulmoograte, Pure Com- mercial .		607, 556	" " c. Caffein ...		780
" " 'A' 1 to 3 gr. per os		607	" Margosate ...		842
" " 'C' 1 to 3 gr. hypod.		607	" Metarsenis ...		181
" Chloras, 10 to 30 gr. ...		773	" Metabisulph. 2 to 5 gr.		781, 277
" Chloridum, 10-60 gr.		766, 277	" Methylarsonas, $2\frac{1}{5}$ to 3 gr.		188
" " Ionisation ...		238	" Methylat ...		774
" chlor-p-acetyl-am. Stibi- nate ...		169	" Molybdate ...		356
" Cinnamas, 3 to 5 gr. ...		25	" Monoboras ...		13
" Citras, 10 to 60 gr.		586, 773	" Morrhuas Solution (3%), $\frac{1}{2}$ to 4 Cc. (Injected) ...		618
" " for Blood Trans- fusion ...		773, 995	" Nitras, 5 to 15 gr. ...		775
			" Nitris, 1 to 2 gr....		775
			" Nitrophenyl-propiolas ...		379
			" Nitroprussidum ...		21, 357

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Sodii Nucleinas, $\frac{1}{2}$ to 2 gr. ...		281	Sodii Thiosulph. Intrav. ...		94
„ Oleas, 2 to 4 gr. ...		761	„ Uras Acidus ...		390
„ „ in cancer ...		761	„ Valerianas, 1-5 gr. ...		825
„ „ in Tuberculosis ...		763	„ Vanadas, $\frac{3}{4}$ gr. ...		892
„ o-coumaras, 5 gr. in sol. ...		27	Sodium ...		766 & 161
„ Palladium Chlor. ...		501	„ Fluorescein ...		678
„ Perboras ...		12, 4	„ Luminal ...		822
„ Permang. ...		555	„ Salvarsan 0.3 to 0.45 Gm. ...		202
„ Peroxidum ...		496, 634	„ Tylmarin, 5 gr. ...		28
„ Persulph., 1 to 3 gr. 779, ...		161, 276	„ Veronal, 5 to 10 gr. ...		819
„ Phenas ...		17	Soil, Iodine in ...		429 <i>et seq.</i>
„ Phenol- <i>p</i> -sulphonas, 5 to ...		19	Solæsthin ...		870
„ Phenol-sulphoricinas ...		621	Solanum, <i>var.</i> , 887; Sodo- mæum ...		887
„ Phenoltetraiodophthalein ...		685	Solazzi ...		860
„ Phenyl glycinamid Ars. ...		209	Soloform ...		21
„ Phenylpropiolas ...		26 & 377	Sols, Colloidal ...		361 <i>et seq.</i>
„ Phosphas., $\frac{1}{4}$ to $\frac{1}{2}$ oz. ...		776	„ „ Iodine ...		371
„ Phosphas Ac., 30 to 60 gr. ...		777, 161	SOLUBES... ..		470
„ „ Eff., 1 to 3 dr. ...		777	„ Antimony Pot. Tart, 10 grs. ...		166
„ „ Exsicc., 10 gr. to 2 dr. ...		777	„ „ Sod. Tart. 10 grs. ...		167
„ „ Neutral (Tribasic) ...		776	„ Antiseptic Dental ...		18
„ Phosphis ...		776	„ Biniodide, 1 in 1 pint=1 in 1,000		465 & 23
„ Pot. Bism. Tart....		239	„ Boric Acid, 15 gr. ...		10
„ Potass. Tart., 2-4 dr. ...		782	„ Borax Co. (et c. Cocaine) ...		10
„ Pyroborate ...		12	„ Boro-Saline ...		10
„ Pyrosulphis, 2-5 gr. ...		781	„ Dental ...		18
„ Rhodanidum ...		782	„ Hyd. Cyanid, et Boracis ...		460
„ Salicylas, 10 to 30 gr. 67, 14, 148, 277, 240		288	„ Hyd. Oxycey, 0.2 Gm. ...		461
„ „ Ionisation ...		760	„ Ionic ...		291
„ Santonas and Santoninas ...		772	„ Perchloride ...		470
„ Sesquicarb. ...		777	1 to tumb.=1 in 4,500 1 in pint.=1 in 1,000 1 in pint.=1 in 500		15
„ Sesquiphos. 30 gr. in die. ...		760	„ Phenol, 5 & 20 gr. ...		706
„ Silicas, 778; Stearas ...		778	„ Plumbi et Opii ...		555
„ Silicofluoride ...		835	„ Potass. Permang., 5 gr. ...		767
„ Succinas, 2 to 5 gr. ...		309	„ Sodii Chlorid. ...		769
„ Sulphanilas, 5-15 gr. ...		779	„ „ Comp. ...		831
„ Sulph., $\frac{1}{4}$ to $\frac{1}{2}$ oz. ...		780	„ Zinc Sulph, et c. Alum ...		20
„ „ Eff., 60 gr. or <i>q.s.</i> ...		780	„ Zn. Sulphocarb., 2 & 10 gr. ...		778
„ Sulph. Exsicc., $\frac{1}{2}$ to 2 dr. ...		779, 277	Soluble Glass ...		984
„ „ Acidus ...		94	Soluro, 5 to 10 gr. ...		Soluté de Chlorure de Sodium
„ Sulph.-hydrate ...		782	Isotonique ...		767
„ Sulphidum ...		781, 277	„ Gelatine Injectable ...		424
„ Sulphis, 5 to 20 gr. ...		781	„ Glucose Hypertonique ...		427
„ „ Exsicc. ...		781	„ „ Isotonique ...		731
„ „ Acid, 5 to 30 gr. ...		782	„ de Quinine hypoderm....		148
„ Sulphocarb., 5 to 15 gr. 19, 240		504	„ de Valer. Ammoniaq. ...		563
„ Sulphocyanid., 1 to 5 gr. ...		621, 240	„ Morphine (HCl.), 2% ...		493
„ Sulph. ichthyol, 10 to 30 gr. ...		782	„ Off. d'Eau Oxygénée ...		140
„ Sulphoricinas ...		238	Solutio Aluminii Acet. ...		352
„ Tart. Neutrale, $\frac{1}{2}$ to 1 oz. ...		782 & 240, 277, 436, 437	„ Amylocain, et c. Gluc. ...		140
„ Tartro Bismuthate ...		12	„ Burowi ...		386
„ Tauro-cholas, 2 to 6 gr. ...		686	„ Creosoti Co. ...		de Cacodyl Iodo-mer- curico ...
„ Tetraborate ...		679, 146	„ Dakin ...		49
„ Tetrabromphenolphtha- lein 4 to 7 Gm. <i>per os</i>		782	„ Ethocaine <i>var.</i> ...		347
„ Tetraiodophenolphthalein 3 to 5 Gm. <i>per os.</i> ...		782	„ Malachite Viridis <i>et</i> Hyd. Perchlor. ...		324
„ See also Iodo-Ray ...		93	„ Phenolis ...		16
„ Thiocyanas ...			„ Salina c. Acac. ...		1
„ Thiosulph., 10 to 60 gr. ...					

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Solutio Tri-iodo phenol	...	21	Spirit Coloniensis	...	118
" Vanillin	...	893	" Creosoti, 1 dr.	...	385
Solvent Naphtha	...	313	" Denaturalised	...	120
Somnifain	...	821	" Dilutions	113, 114 & 22	
Somnifen	...	821	" Duty and Rebate	...	114
Somnoform	...	111, 836	" Frumenti	...	118, 26
Soneryl, 1 to 2 gr., 821; Tabs.,	...	821	" Glycerin	...	117
1 gr.	...	821	" Glyceryl Nit., av. 1 m.	...	577
Sorbefacin	...	431	" Grindeliæ Co., 1 to 2 dr.	...	444
Sorbus, 887; Sorghum	...	887	" Hyd. Biniodidi	...	463
Sorrel	...	167	" Isopropyl	...	125
Soudan Red III.	...	326	" Juniperi, 5 to 20 m.	...	865
Soya	...	619, 887 & 388	" " Co., U.S., 2 dr.	...	865
Spanish or Blistering Fly	...	267	" Lavandulæ (10% of Oil),	...	
" Glossary	...	643	5 to 20 m.	...	
Spahlinger's Serum	...	946	" Melissæ Co., 20-25 drops	...	870
Spas and Health Resorts	...	459	" Menthæ Pip., 5 to 20 m.	...	870
Spasalgin Tabs. and Inj	...	569	" Methylatus, 120; Indus-	...	
Spasmine, 5 to 15 gr.	...	312	trial	...	120, 121
Spasmodin, 2 to 6 m. (in solution)	...	311	" Myrciæ	...	113
Sparteinae HCl, Sulph. $\frac{1}{2}$ to 1 gr.	...	784, 240	" Myristicæ, 5 to 20 m.	...	871
Sparteine Period, $\frac{1}{2}$ to 3 gr.	...	135, 784	" Nuc. Jugl., 1 to 4 dr.	...	864
Spearmint	...	870	" 'Power	...	122
Spermatozoa	...	615, 616	" Prohibition	...	117
Species Pectorales	...	860	" Proof	...	114 & 23
Spengler's Method	...	598	" Rebate	...	114
" Tuberculin	...	945	" Rectificatus	...	113 & 23
Spermaceti	...	849	" Saponatus, var.	...	762
Speton Tabs.	...	729	" Sinapis, P.G. V.	...	764
Sphagnol and Preps.	...	505, 761	" Surgical	...	120
Sphagnum (<i>see also</i> Moss)	...	785	" Tenuior	...	114 <i>et seq.</i>
Sphygmograph, Varnish	...	7	" Thymol, 3 to 15 m.	...	812
Sphygmomanometers	...	402	" Vanillin Co., $\frac{1}{2}$ to 1 dr.	...	893
Spigelia Marilandica	...	888	" Varnish	...	122
Spinach	...	100, 106	" Vini Rect. & Dilutus	...	113 & 22
Spinal Anæsthesia. <i>See</i> An-	...		" Vitis	...	118
æsthesia & Drugs in question.	...		Spirits Act, 1915	...	114
Spinal Cord Ext. (5-20 m.)	...	959	Spirochæta, Pallida, 196,	...	574;
" " Tabs., 2 $\frac{1}{2}$ gr.	...	959	Staining	...	575 <i>et seq.</i>
Spirillum Cholerae	...	913	Spirochæta, Duttoni	...	585
" " Obermeieri	...	568	" Recurrentiss	...	566
<i>See also</i> Spirochæta.	...		" var.	...	575-578
Spirit Weed, 866; of Tar	...	704	" pallidula	...	612
Spirit Acidi. Lactici	...	55	Spirochætosis icterohæmorrhagica	...	610
" Adhesive Resin	...	869	Spirocid, 4 grains	...	192
" Aetheris, 60 to 90 m.	...	109	Spirochætosis, 196, 574;	...	
" " Camph.	...	383	Staining	...	575 <i>et seq.</i>
" " Co., 60 to 90 m.	...	109	Spleen Desicc., 5 to 10 gr.	...	974
" Aether. Nit., 15 to 60m.	...	109, 22	Splenomegaly, Tropical, v. Kala	...	
" Ammon. Aromat., 60 to	...		Agar.	...	
90 m.	...	150	Splints, Celluloid	...	361
" " Fetidus, 60 to 90 m.	...	150	Spodumene	...	334
" Amygd. Amar., av. 8 m.	...	152	Sponge Education	...	437
" Anisi, 5 to 20 m.	...	840	Sponges, Surgical	...	437
" Antiparalyticus	...	701	Spongio Piline	...	436, 437
" Armoraciæ Co., 1 to 2 dr.	...	852	Sporotrichosis	...	572
" Aurantii Co., U.S.	...	401	Spot Wing, A. Maculipennis	...	557
" Cajuputi, 10%, 5 to 20 m.	...	845	Spotted Fever	...	909, 572
" Camphoræ, 5 to 20 m.	...	263, 54	Sprays (Cocaine)	...	338
" " Fort., 2 to 5 m.	...	264	Sprue	...	858 & 572
" Capillaris	...	751	Spruce, Hemlock	...	878
" Card Co.	...	639	Spurge, Petty	...	857
" Chloroformi, 5 to 40 m.	...	290	Squaw Root	...	848
" Cinnamomi, 5 to 20 m.	...	298	Squill 885, 74; Red, 885; Indian	...	892
			Stabilarsan	...	202

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Stabilised Tinctures ...		824, 836	Sterules, Hypodermic—<i>contd.</i>		
Staining Methods ...		614	Aconitine Nit., 1/600 gr. ...		100
Staniform ...		168	Adrenalin Sol., 10 to 15 m. ...		981
Stainless Iodine Ointment ...		516	Adrenalin Solution, 1/1000 gr.		
Stains, To remove ...		638	with Cocaine, $\frac{1}{4}$ gr. ...	339,	981
Stamm's Test ...		21	Adreucaine, $\frac{1}{2}$ Cc. ...		344
Stamp Medicine Concession ...		624	Æther, $\frac{1}{2}$ dr. ...		103
Stannum ...		888	Amyl Nitrite, 15 m., hyp.		
Stanni Oleas ...		604	dose, 1 to 5 m. ...		157
" Oxid ...		888	See also Sterules, Inhalation.		
Stannoxy Tablets ...		888	Antimon Ox. Inj., 15, 30 m. ...		158
Staphisagriæ Oleum & Ung. ...		888	" Pot. Tart. $\frac{1}{2}$ to 2 gr.		
" Sem., 1 gr. ...		888	(Intrav.) ...		165
Staphylo. Alb., Aur. & Vaccine ...		930, 573	" Sod. Tart. $\frac{1}{2}$ to 2 gr.		
Star Anise ...		840	(Intrav.) ...		166
Star Grass ...		837	Antipyrin, 4 gr. ...		328
Starchy Foods ...		586-588	" et c. Cocaine, 1/20 gr. ...		329
Starch, 339; and Boric. Powders ...		829	Apomorph. HCl., 1/10 gr. ...		171
" Indicator ...		189	Aq. Dest., 1 dr. ...		217
Starchless Bread ...		591	Arrhenal, $\frac{1}{2}$ and $\frac{3}{4}$ gr. ...		188
Static Electricity ...		312	Arsamin, $\frac{1}{2}$ and $\frac{3}{4}$ gr. in 15 m. ...		190
Stavesacre ...		888	Arsenic and Iron = $\frac{1}{2}$ and 1		
Steapsin ...		637, 76	mgr. As ₂ O ₃ , in 15 m. ...		183
Stearettes... ...		697	" and Strychnine = 10 m. ...		185
" Calcii Sulphidi, 1 gr. ...		261	" Strychnine & Quin. 10 m. ...		185
" Emetine HCl. $\frac{1}{2}$ & $\frac{3}{4}$ gr. ...		531	Arsenii Iodidi, 1/100 gr. ...		183
" Emetine Bism. Iodid.,			Atrop. Sulph., 1/100 gr. ...		214
1, 2 & 3 gr. ...		532	Atropine Sulph. $\frac{1}{100}$ gr. c.		
" Fæxin Ext. ...		230	Strych. $\frac{1}{36}$ gr. ...		500
" Fel Bovini, 5 gr. ...		411	Auri Chlor. (<i>see also</i> Gold		
" Iodo-Ray 0.3 & 0.5 Gm. ...		680	Colloid) ...		219
" Magnesium Peroxid., 3 gr. ...		496	Becker's Solution ...		46
" Sulphur, 5 gr. ...		798	Benzamine, $\frac{1}{2}$ and $\frac{1}{2}$ gr. ...		344
" Trypsin 5 gr. ...		639	Bismuth Metal 0.2 Gm. ...		242
" Other Comps. ...		697	Bismuth Sod. Pot. Tart. 3 gr. ...		242
Stearoptene, Otto ...		167	Bismuth Salicyl 2 gr. ...		232
Stearin ...		91	Bismutol ...		242
Stedman's and Steedman's			Butyn 1 & 2%, 1 Cc. ...		355
Powders ...		635	Cacodylatum Co., 15 m ...		188
Stegomyia calopus, fasciata ...		612	Caffeine and Novocain ...		348
Steinach Operation ...		983	Caffeine Sod. Benz. 3 gr.		
Sterilla ...		762	Intrav. ...		251
Sterilisation of the Skin 470, 480, ...		518	" 2 gr. in 1 Cc. & 5 Cc.		
Sterilisation, Chapter ...		257	Intrav. ...		251
Sterilised Milk 587 <i>et seq.</i> ;			" Sod. Sal., 1, 2 gr. ...		251
Olive Oil, Paraffin, etc. ...		152	Calcii Format., $\frac{3}{4}$ gr. ...		35
Sterilisers ...		587	Calc. Glyceroph., 1, 2, 3, 4 gr. ...		37
" Tubes for ...		261	Calomel, $\frac{1}{2}$, $\frac{1}{4}$, $\frac{1}{8}$, $\frac{3}{8}$ and 1 gr. ...		475
"Steriloid" Dressings... ...		437	Camphor (in oil), $1\frac{1}{2}$ and 3 gr. ...		263
Steriloids.			" $\frac{1}{4}$ gr. in Ether, 15 m. ...		263
Atropine 1/400, 1/200, 1/100			Camphor, 3 gr. & Guaiacol, 2 gr. ...		263
gr. ...		134	Cicatricine, 15 m. ...		765
Cocaine 1/60, 1/50, 1/30 gr. ...		134	Cinchonidine HCl. Ac. 7 $\frac{1}{2}$ gr.		
Codeine 1/16, 1/4, 2/7 gr. ...		134	(Intram.) ...		723
Diamorphine 1/50, 1/30 gr. ...		134	Cocaine HCl., 1/10, $\frac{1}{2}$ and $\frac{1}{4}$ gr. ...		339
Emetine, 1/18, 1/14, 1/9 gr. ...		134	" $\frac{1}{2}$ & Adrenalin, 1/1000		
Morphine, 1/160 gr. ...		134	gr. (Conephrin) ...	339,	981
Quinidine, 1/60 gr. 1/50 gr. ...		134	Cocaine et Sod. Bic., Dry		
Quinine ...		134	(Urethral) ...		339
Strychnine, 1/360, 1/180, 1/90			Codeine Phosph., 1 gr. ...		357
gr. ...		134	Colloidal Metals, <i>see</i> "Sterules"		
Sternberg's Mixture ...		1038	of Metals in question		
STERULES, HYPODERMIC.			Copper Colloidal, 4 Cc. ...		370
787, each containing:—			Creosote (in oil), $\frac{1}{2}$ gr. ...		—
Acac. Gum (Intrav.) ...		1	Curschmann's Soln., 1 Cc. ...		264

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Sterules, Hypodermic—<i>contd.</i>			Sterules, Hypodermic—<i>contd.</i>		
Diamorphine, HCl., 1/12 gr.	...	566	Lecithin c. Guaiacol, $\frac{1}{4}$ gr.	...	540
Digitalin, Pulv., 1/10 gr.	...	400	„ c. Strych., 1/120 gr.	...	540
„ 1/10 gr. c. Strych. HCl.	Locke's Soln. Conc.	...	767
„ 1/100 gr.	...	400	Mang. Butyrat., 1%, 1, 1 $\frac{1}{2}$
Dionin, $\frac{1}{4}$ gr.	...	566	and 2 Cc.	...	552
Emetine HBr., $\frac{1}{4}$ & $\frac{1}{4}$ gr.	...	531	Mannitol-Quinine, 2 Cc. (?)	...	734
„ HCl., $\frac{1}{4}$ to 1 gr.	530, 561	...	Menthol, 1/5 gr.	...	557
Enesol, 2 Cc.	...	139	Mercurial Injn., 10 m.	...	454
Ergot Inj., 10 m.	...	405	Mercuriome, 0.3 Gm., vesical
Eucaïn, HCl. & Lact., $\frac{1}{4}$, $\frac{1}{4}$	inj.	...	480
and 1 gr.	...	344, 345	„ 0.2 Gm. Intravenous	...	480
Eucaine & Sod. Chlor. (Dry-	...	344	Mercury Salicylate, 1/10 to
filled)	...	344	1 gr.	...	473
Eucalyptus Oil., 5 m. c. Ol.	...	615	Methylene Blue	...	62
Ferri Am. Cit., $\frac{1}{4}$, 1 & 2 gr.	Milk, 5 & 10 Cc. (intram.)	...	676
(and both c. Strych., 1/60	Morph. Sulph., $\frac{1}{8}$, $\frac{1}{4}$, $\frac{1}{4}$, & $\frac{1}{2}$ gr.	...	564
gr.)	...	412	Morph., $\frac{1}{4}$ gr. c. Atropine
Ferri Glyceroph., $\frac{1}{4}$ gr.	...	37	Sulph., 1/120 gr., and $\frac{1}{4}$ gr.	...	564
Fibrocoumarin, 25 m.	...	27	c. $\frac{1}{100}$ gr.	...	767
25 m. c. Adrenalin, 10 m.	...	27	Normal Saline (conc. 371)	...	347
Gelatin Cone.	...	424	Novocain, $\frac{1}{4}$ gr.
Glucose (Intrav.)	...	427	„ $\frac{1}{4}$ gr. c. Adrenalin,	...	347
Glyc Sod. Cinnam.	...	26	1/1000 gr.
Gold Coll., 5 Cc. (1 in 4000)	...	371	„ 0.15, Caffeine 0.12 and	...	348
Guaiacol (in oil) $\frac{1}{4}$ gr.	...	446	Sod. Benz. 0.15 Gm.	...	281
„ Cacodyl., $\frac{1}{4}$ to 2 gr.	...	186	Nucleinic Acid, $\frac{1}{4}$ gr.	...	606
„ Camphor & Iodine, $\frac{1}{4}$	Oleum Chaulmoogræ	...	700
and 1 Cc.	...	446	Ol. Terebinth in Oil...	...	669
Guaiacol-Glucose, 2 Cc. for	Peptone Intramusc., graded	...	669
Novarsenobenzol	...	205	„ „ cont., course	...	668
Gum Acac. (Intrav.)	...	1	„ Intrav., graded	...	668
Hamamelis Ext. and Phenol.	...	449	„ „ cont., course	...	668
Hydrarg. Coll., 5 Cc. (1 in	...	375	„ and Shading off	...	672
2000)	„ in Vaccine Therapy	...	672
Hyd. Cyanid. 1/12, $\frac{1}{4}$ gr.	...	460	„ 10% in Septicæmia	...	63
(Intrav.)	...	460	Phenolsulphonaphthaleïn	...	688
Hydrarg. Lambkin, 10 m.	...	454	Phosphorated Oil, 5 minims	...	696
Hyd. Glycocoll., $\frac{1}{4}$ gr.	...	5	and $\frac{1}{4}$ m. in 5 m. Oil	...	968
„ Iod. Rub., 1/12 gr. in 8m.	...	463	Pilocarpine Nitrate, 1/10, $\frac{1}{4}$, $\frac{1}{2}$ gr.	...	968
„ Salicyl., $\frac{1}{16}$ to 1 gr.	...	473	Pituitary Ext. (Infundib.),
„ Salicyl-Arsonas, 1 gr. in	...	139	$\frac{1}{4}$ and 1 Cc.	...	968
30 m.	...	475	Pituitary Ext. (Anterior), 1	...	968
„ Subchlor., $\frac{1}{4}$, $\frac{1}{4}$, $\frac{1}{4}$, 1 gr.	...	476	and 2 Cc. (20 and 40%)	...	968
„ Succinimid., $\frac{1}{4}$ gr. c.	...	476	Pituitary Extract, $\frac{1}{4}$ and 1 Cc.	...	968
Cocaina Nit., $\frac{1}{4}$ gr.	...	493	Entire Gland Special	...	375
Hydrastinine HCl., $\frac{1}{4}$ & $\frac{1}{4}$ gr.	...	500	Platinum Coll., 5 Cc. (1 in 4000)	...	716
Hyoscine HBr., 1/100 gr.,	...	500	Potass. Iod., 5 gr.	...	727
500; et c. Morph., $\frac{1}{4}$, etc.	...	500	Quin. Formas, $\frac{1}{4}$, $\frac{1}{4}$ grain	...	38
Hyoscine Comp.	...	500	„ Glyceroph., $\frac{1}{4}$ gr.	...	728
„ Hyoscyamine HBr.,	...	502	„ HBr. Acid, 2 gr.	...	731
1/100 gr.	...	454	„ HCl. Acid, 2 gr., 3 gr.,	...	731
Inj. Hydrarg. Intramusc., 10m.	...	518	5 gr. and 15 gr.	...	731
Iodine (local)...	...	62	„ 4 & 10 gr. Intrav.	...	731
Indigo Carmine	...	519	„ „ 5 gr. c. Anti-	...	732
Iodinol, 30 & 60 m.	...	508	pyrin, 3 gr.	...	734
Iodoform c. Menthol...	...	412	„ Hydrochlorocarbamid.,	...	243
Iron and Arsenic—	3 and 5 Cc., 1%	...	732
No. 1 = $\frac{1}{4}$ mgr. As ₂ O ₃	...	183	„ Mannitol, 2 Cc. (?)	...	734
No. 2 = 1 mgr.	...	412	„ Iodo-Bismuthate, 0.17
Iron Citrate, $\frac{1}{4}$, 1 and 2 gr.	...	412	Gm.	...	732
„ „ $\frac{1}{4}$, 1 & 2 gr. with	...	37	„ Urea (& c. Eucaine),	...	741
Strychnine, 1/60 gr.	...	540	and 5 Cc.
„ Glyceroph., $\frac{1}{4}$ gr.	„ Urethane (for veins),
Lecithin, $\frac{1}{4}$ gr.	2 Cc.

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Sterules, Hypodermic—<i>contd.</i>			Sterules, Hypodermic—<i>contd.</i>		
Quinidine HCl. Ac. 5 and 10 gr.			Urea-Quinine and c. Eucaine		732
(Intrav.)...		722	Water Distilled, 5 Cc.		217
" " 5 gr. Intram.		722	STERULES, INHALATION		787
Ringer's Sol. Conc. ...		767	Ammonia 3 m.		148
Saline Conc., for Gold, 371;			Amyl Nitrite, 1 to 10 m.		153
for 2 pints....		767	Chloroform, 10, 20, 30 and		
Scopolamine-Morph., 1/100			60 m., also 1, 2, 4 oz.		
and $\frac{1}{2}$ gr., and with Atrop.		500	(Anæsthetic) ...		289
Selenium Coll., 1 to 5 Cc. (1			Ether, 1 and 2 oz. ...		102
in 5000) ...		376	Ethyl Bromide, 5 m.		836
Silver Coll. 5 Cc. (1 in 2000)		376	Ethyl Iodide, 5 m.		112
Sod. Arsenatis et Strych., 10m.		185	" c. Chlorof.		112
" " et Quin., 10 m.		185	" " et Menthol		113
" Bicarbonate, 3 Gm.			Trichlo"ethylene, 10 m.		292
(Intrav.) ...		771	STERULES, IONIC ... 787 &		291
" Chloride ...		767	STERULES LOTION for diluting		
" Conc. for Coll. Gold 371;			1 to 1 pint:—		
for 2 pints ...		767	Hydrarg. Perchlor. ...		470
" Cacodyl, $\frac{1}{2}$, $\frac{3}{4}$, 1, 1 $\frac{1}{2}$ and			" Biniodid ...		465
2 gr. ...		188	" Oxycyanid ...		461
" " 1 gr. in Nuclein			Potass. Permang. ...		555
Soln., 1 Cc. ...		188	Saline Soln. (for 2 pints)		767
" Sod. Chaulmoog.			STERULES, OPHTHALMIC		787
" 'C,' 1, 2, and 3 gr. ...		608	Adrenalin Chlor. ...		981
" Cinnam. (Glyc., 30 m.)		26	Atrop. Sulph., 1% ...		214
" Formate, $\frac{1}{2}$, $\frac{3}{4}$ gr. ...		35	" Sulph., $\frac{1}{2}$ % with Cocaine		214
" Glyceroph., 3 gr. ...		38	Cocaine HCl., 10 gr. to oz.		
" " 1 $\frac{1}{2}$ c.Strych. Cacodyl.,			(& tube form) ...		339
1/64, 1/20 gr. ...		38	Dionin, 5% ...		565
" Hydnocarpat., 10 Cc.,			Fluorescein et Sod. Bic. ...		678
1% ...		611	Holocaine, 1% ...		345
" Hyposulph., 0.2, 0.45			Homatropine, HBr., 1%		
and 0.6 Gm. <i>intrav.</i>		94	(et c. Cocaine, 2 $\frac{1}{2}$ %) ...		217
" Iodid. 1 gm. (Intrav.)		775	Physostigmin., 4 gr. to oz. ...		694
" Nitritis, $\frac{1}{2}$, $\frac{3}{4}$, $\frac{1}{2}$ gr. ...		775	" 1 gr., et c. Coc., 4 gr. ...		694
" Nucleinate, $\frac{1}{2}$ gr. ...		281	Pilocarpine Nit., 0.5% ...		695
" o-Coumarate Sol., 25 m.		27	Protargol, 10 and 25% ...		177
" " c. Kerocain, 1/5 gr.		27	STERULES, LARGE (TUBE		
" " et Adrenalin, 10m.		27	FORM) 10 min., Cocaine		
Sod. Pot. Bism. Tart. 3 gr.		242	HCl., 5, 10% ...		339
" Salicyl., 1 Gm. (and c.			Stibamine Compds. ...		168
Sod. Iod. 1 Gm.) (<i>Intrav.</i>)		71	Stibenyl $\frac{1}{2}$ gr. (Intrav.)		168
" Salicyl. 1 Cc. 30% for			Stibium Sulph. ...		157
hæmorrhoids ...		70	Stibnite ...		157
" " 3 Cc. of 20, 30 and			Stibosan ...		169
40% for varicose veins		70	Stillingia, 30 gr.		888
Stovaine, $\frac{1}{2}$, $\frac{1}{4}$, $\frac{3}{4}$ gr. .		350	Still's Diplococcus ...		911
c. Caffeine ...		353	Stinging Nettle ...		34
" Glucose Sol., 1 Cc. ...		351	Stockholm Tar 2 to 10 gr.		703, 149
" Strychnine, 1 Cc. ...		353	Stockman on Salicylates		68 <i>et seq.</i>
Strophanthin, $\frac{1}{4}$ to 1 mgr.			Stokes' Liniment ...		700
(<i>Intrav.</i>) ...		790	Stomach Contents Exam.		413
Strych. Formate, 1/60 gr. ...		36	" Tubes ...		271, 414
Strych. Sulph., 1/100, 1/50 gr.		794	Stomachic balsam ...		872
Sulphur Coll., 5 Cc. ...		377	Stomonal ...		61
Sulphur 0.001 Gm. in oil ...		797	Stone Root ...		852
Testicular Ext. c.Glyceroph.,			Storax ...		888
2 gr., c. Strych., 1/60 gr. 10 m.		983	Storks-bill ...		856
Thiosinamin, Comp., 1 & 2 Cc.		765	Stout ...		26
with Antipyrin = 15 m. ...		765	Stovaine, $\frac{1}{2}$ to $\frac{3}{4}$, max. 2 $\frac{1}{2}$ gr.		
Tuberculin Dilutions		938 <i>et seq.</i>	350, 69, 240; Stovaine-Dex-		
Turpentine in Oil ...		700	trin, 352; Gargle, Ointment,		
Tylcalsin 0.5 and 1 Gm.			Pastils, Snuff, Soln. (internal)		353
(<i>Intrav.</i>) ...		78			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE
Stovaine-Caffeine	353
Stovaine-Glucose	351
Stovaine-Strychnine	353
Stovarsol, 4 grs., 192, 536, 537, 538	...	538
<i>Stramonium</i>	787
Strawberry	858
Streptococcus <i>var.</i> & Serum	928, 573	
Conglomeratus	929, 574	
Hæmolytic, 930; and		
<i>see</i> Influenza.		
<i>fæcalis</i> ...	928 & 573	
<i>Lebenis</i> ...	11	
<i>pyogenes</i> ...	573	
<i>Rheumaticus</i> ...	927	
<i>Salivarius</i> ...	573	
Strong's Method ...	396	
Strontium ...	788	
<i>Strontii Brom.</i> (Exsicc., 4-24		
gr., 789); 5-30 gr. ...	788	
<i>Carb.</i> , 5 to 30 gr. ...	789	
<i>Chlorarsinobenolate</i> ...	189	
<i>Cinnam.</i> , 2 to 5 gr. ...	26	
<i>Glyceroph.</i> , 4 to 8 gr. ...	39	
<i>Iodid.</i> , 5 to 20 gr. ...	789	
<i>Lactas.</i> , 5 to 30 gr. ...	789	
<i>Oleas</i> , 5 to 20 gr.(?) ...	604	
<i>Salicyl.</i> , 5 to 20 gr. ...	789	
<i>Sulphidum</i> ...	222	
<i>Strophanthi Semina</i> ...	789, 161	
<i>Phys. Std.</i> 791 & 74, 161		
Strophanthidin ...	790	
Strophanthin, 1/300 to 1/100		
gr. ...	790, 240	
<i>Strychnina</i> , 1/64 to 1/16 gr. ...	791	
Antidotes ...	792	
Ionisation ...	289	
Tests ...	123, 242	
<i>Strychninae</i> <i>Acetas</i> , 792;		
<i>Arsenas</i> , 1/64 to 1/16 gr.,		
792; <i>Cacodylas</i> , 1/30 to 1/10		
gr., 188; <i>et Fe. Cit.</i> 2 gr. 792;		
<i>et Fe. Quin. Cit.</i> 3 to 6 grs.,		
792; <i>Formas</i> , 1/64 gr., 35;		
<i>Glyceroph.</i> , 1/64 to 1/20 gr.,		
39; <i>HBr.</i> and <i>HCl.</i> 793, 277		
<i>Strychnin</i> , <i>Hypophosph.</i> , 792;		
<i>Nitras</i> , <i>Phosph. Acid.</i> , <i>Sulph.</i>		
and <i>Sulph. Acid.</i> , 1/64 to		
1/16 gr., 793, 794; <i>Periodid</i> ,		
1/100 gr., 135, 794; <i>Valeria-</i>		
<i>nas</i> , 1/25 to 1/10 m. ...	794	
<i>Strychnos</i> , <i>var.</i> ...	598, 599	
<i>Styptic Colloid</i> , 361; <i>Gelatin</i> ,		
981; <i>Wool</i> ...	413	
<i>Stypticin</i> , 1, 1/2 gr., or if urgent		
up to 4 gr. ...	573	
<i>Stypticin Gauze and Wool</i> ...	574	
<i>Styptol</i> , 1/2 gr. <i>incr.</i> ...	574	
<i>Styrax Prep.</i> , <i>av. U.S.</i> , 15 gr.	888	
<i>Styryl Quinoline</i> ...	317	
<i>Sublimate Disinf.</i> , 470; <i>Mala-</i>		
<i>chite Green Soln.</i> , 324, 471;		
<i>Spirit</i> , 470; <i>Gauze, Wood Wool</i>	469	
<i>Succinimide</i> ...	476	
<i>Succinum</i> ...	889	

NAME.	DOSE.	PAGE
<i>Succus Agavæ Conc.</i> , 1/2 oz.	879
<i>Allii</i> , 10 to 30 m.	837
<i>Alterans</i> , 1 dr.	888
<i>Ari</i> , 1 dr.	842
<i>Conii</i> , B.P. '98, 1 to 2 dr.	...	858
<i>Galii</i> , 1 to 2 dr.	858
<i>Limonis</i> (<i>see</i> <i>Neutralisa-</i>		
<i>tion Table</i>)	
<i>Mori</i> , 1 dr.	871
<i>Nasturtii Off.</i> 2 to 4 dr.	873
<i>Papav. Somnif.</i> (<i>Cap.</i>		
<i>Inspiss.</i> (and <i>Pulv.</i>),		
1/2 to 2 gr.	625
<i>Scoparii</i> , 1 to 2 dr.	886
<i>Semperviv.</i> , 5 to 15 m.	890
<i>Taraxaci</i> , 1 to 2 dr.	34
<i>Urticæ</i> , 1 to 4 dr., <i>incr.</i>	76
<i>Sucrase</i>	757
<i>Sucrose</i> , <i>Sugar</i> , 755, 157, 242;		
<i>Intrav. use</i>	326
<i>Sudan Red</i>	755
<i>Sugar Beet</i> , 755; <i>Cane</i> , 755;		
<i>Chinese</i> , 887; <i>Coating</i> , 697;		
<i>Grape</i> , 426; <i>Inverted</i> 757;		
of lead 705; <i>Subsidy</i>	606, 607
<i>Sugars</i> , <i>Bacteriological</i>	757
<i>Relative Sweetness</i>	207
<i>Sulfarsenol</i>	799
<i>Sulphaqua Charges</i>	207
<i>Sulpharsenobenzene</i>	207
<i>Sulpharsphenamine</i>	222
<i>Sulphate de Ba. Gelat.</i>	242
<i>Sulphonal</i> , 10 to 30 gr. 795 & 277, 242		
<i>Reversed</i>	795
<i>Sulphone-ethyl-methane</i>	795
<i>Sulphoxyl-Salvarsan</i> , 8-12 Cc. 208		
<i>Sulphonmethanum</i>	795
<i>Sulphur</i>	796
<i>Sulphur. Lime Depilatory</i>	261
<i>Colloidal</i> 366, 377, 797		
<i>Sulphur Dioxide and Trioxide</i> 93		
<i>Sulphurated Potash v. Potass.</i>		
<i>Sulphurata</i>	798, 500
<i>Sulphuretted Hydrogen</i>	798
<i>Sulph. Chlor.</i> , <i>Hypochlor.</i>	797
<i>Sulph. Injections</i>	798
<i>Iodidum</i>	797
<i>Lotum</i>	797
<i>Paste</i>	796
<i>Præcip., Sublim.</i> , 20 to		
60 gr.	316
<i>SUM Compds.</i>	882
<i>Sumach</i> , 15 gr.	882
<i>Smooth</i> , 15 gr.	889
<i>Sumbul Radix. av.</i> 30 gr.	854
<i>Sundew</i>	619
<i>Sunflower Oil</i>	293
<i>Sunic Coil</i> , 291; <i>Screens</i>	321
<i>Sunlight</i> ...	596 & 278, 321	
<i>SUP Compds.</i>	316
<i>Superol</i>	316
<i>Supplementary Drug Lists</i> 832, 164		
<i>Suppositories</i> , 800; <i>Hollow</i>		
431; <i>Mass for hot Climates</i> ,		
800; <i>Vaginal</i>	431

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Suppos. Acidi Borici, 3 gr. ...		11	Suprarenal Gland, 974, 170;		
" " Carbol., 1 gr. ...		18	Ext. Dry, Liq., Suppos. (et.		
" " Lact. B. ...		59	c. Morph., $\frac{1}{2}$ to 3 gr.), Inj.		
" " Tannici, 3 gr.,			(Hypod.), Snuff, Insuff. Pdrs.,		
and with Morph.,			Nebula, Spray, Tabellæ,		
$\frac{1}{2}$ or Opium, 1 gr. ...		95	Tablets 1 or more, Ung.,		
" Adrenalin, 10 m. ...		981	975 <i>et seq.</i> ; Assay ...		170
" " c. Formidin. Co-			Suprarenin ...		976
cain & Hamam. ...		981	" Synthetic ...		977, 171
" Aloes ...		139	Suprarenalum Sicc. U.S. ...		975
" Argyrol ...		176	Supsalvs. ...		199
" Aristol, 1 gr. ...		510	Surgeon's Agaric ...		838
" Arsenobenzol ...		199	Surgical Dressings 437, 438, 261		
" Atropinæ et Plumbi Iod. ...		215	Surgical Lubricant ...		16
" Bellad., $1\frac{1}{2}$ gr. ...		226	Surgical Soap ...		761
" " et Morph., $\frac{1}{4}$ gr. ...		226	Surgical Spirit ...		120
" Bisciniod, $\frac{1}{4}$ gr. ...		231	Suspension d'Iodobismuthate		
" Bismuthi Oxychl., 10 gr. ...		232	de Quinine, 1 Cc. ...		243
" " Salicyl., 10 gr. ...		233	Suspensoids ...		362
" " Subnit., 10 gr. ...			Sutures ...		542
" Chloral, 5 gr. ...		283	Swabs, Steriloid, Triang. etc. ...		437
" Chrysarobin, $1\frac{1}{4}$ gr. ...		295	Swartz's Medium ...		549
" Cocainæ, $\frac{1}{2}$ to $\frac{1}{4}$ gr., et c.			Sweetbread ...		637
Morphina, $\frac{1}{2}$ gr. ...		339	Sweet Gale, 844; Vernal Grass ...		841
" Cocainæ Vaginal, 2 gr. ...		339	Sydenham's Laudanum, 5 to		
" Collargol (& Co.), $2\frac{1}{2}$ gr. ...		176	20 m. ...		631, 138
" Collinson Ext. ...		852	Syls, 1 to 2 drachms:—		
" Cubebæ, 10 gr. ...		853	Amygd., Anethi, Anisi,		
" Eucalypti Gum, 5 gr. ...		856	Aurant. Amar., Aurant.		
" Ext. Myrtilli ...		872	Flor., Carul, Caryoph.,		
" Gallæ, 5 gr., et c. Opio, 1 gr.			Cinnam., Fœniculi, La-		
<i>Glycerini</i> ...		481	vand., Limonis, Menth.		
" Hæmorrhoidal ...		236	Pip., Menth. Vir., Myrist.,		
" Hamam Co. ...		449	Pimentæ, Pini, Rosæ,		
" Hamamelin, 1 and 3 gr. ...		449	Thymi, Vanillæ.		
" " et Hydrarg. Co. ...		449	Symmetrical Urea Compds. ...		316
" Hamam., Conii et Eucain ...		449	Symphytum var. ...		889
" Hydrargyri ...		455	Synergism of chemicals with		
" " Subchlor., 1 gr. ...		475	Morphine, etc. ...		107, 569
" Ichthosulphol, 3 gr. ...		504	Synol Soap ...		762
" Iodex ...		516	Synthallin ...		650
" Iodoformi, 1, 3, 5 gr. ...		509	Synthetic Milk ...		887
" " c. Eucalyp. Oil., 5 m.			Syphilis 194, 454 and 1092, 574		
" Malourea, 4 to 8 gr. ...		817	" Arsenic & Mercury		
" Morphinæ, $\frac{1}{4}$ gr. ...		563	comb. treatment ...		199
" Novarsenobenzol, 0.1 Gm. ...		207	" Benzoin Reaction ...		410
" Novocain, $1\frac{1}{2}$ grains ...		348	" Bismuth in ...		240
" Olei Cinerei ...		455	" Complement Deviation ...		579
" Opli, 1 gr. ...			" Diagnosis Methods ...		574
" Quassia Ext., $\frac{1}{4}$ gr. ...		880	" Kahn Test for... ...		583
" Quin. HCl., 5 gr....		728	" Mastic Test for ...		410
" " HCl. Carbam., 5 gr. ...		732	" and Parasyph. differtn. ...		409
" Ranunculi ...		881	" Sach's Test for ...		583
" Salvarsan... ...		199	" Salvarsan in ... 194 <i>et seq.</i>		
" Santoninl, 3 gr. ...		760	" Targowla Reaction ...		584
" Sod. Chaulmoograte ...		607	" Verne's Test ...		584
" Sonéryl, 0.1 Gm. ...		821	" War Office Treatment ..		199
" Supra-renal (et c. Morph.) ...		976	" Wasserman Reaction... 579		
" Thymol Iodide ...		510	Syringes Hypod. ...		455
" Veronal, 4 to 8 gr. ...		817	<i>Syrupus</i> ...		757
" Veronal Sodium, 0.4-0.5			" Acid Hydriodic, 30 to 60m. ...		41
Gm. ...		820	" Ægle Marim. Co., $\frac{1}{2}$ to 1 oz. ...		844
Supplementary List ...		832, 164	" Apomorph. HCl., $\frac{1}{2}$ to 1 dr. ...		171
Suprarenal Cort., 2-5 gr. ...		982, 171	" Aromat., $\frac{1}{2}$ to 1 dr. ...		
			" Aurantii, $\frac{1}{2}$ to 1 dr. ...		842

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Syrupus Benzaldehydi HCN.	$\frac{1}{2}$ to 1 dr.	879	Syrupus Tolu.,	$\frac{1}{2}$ to 1 dr.	843, 881
„ Bromoformi, $\frac{1}{4}$ to 1 oz.	...	246	„ Triplex, 1 to 2 dr.	...	420
„ Calcii et Fe. Lactoph.,	$\frac{1}{2}$ to 1 dr.	56	„ Trium Phosph., $\frac{1}{2}$ to 1 dr.	...	419
„ „ Lactoph. $\frac{1}{2}$ to 1 dr.	...	56	„ Erginæ, $\frac{1}{2}$ to 1 dr.	...	892
„ Camph. Co., 1 dr.	...	630	„ Violæ, ad lib.	...	894
„ Cascaræ Aromat., $\frac{1}{2}$ -2 dr.	...	277	„ Zingib., $\frac{1}{2}$ to 1 dr.	...	895
„ Chloral, $\frac{1}{2}$ to 2 dr.	...	283	Sys Specific	...	253
„ Cocainæ, 1 dr.	...	339	Sysimbrium	...	856
„ Cocillanæ Co., $\frac{1}{2}$ to 1 dr.	...	351	Systogen	...	407
„ Codeinæ Phosph., $\frac{1}{2}$ to 2 dr.	...	357	T. A. B. Vaccine	...	948
„ Cyllin, 10 to 60 m.	...	32	T.A.B.C. Vaccine	...	949
„ Digitoxin, 1 to 4 dr.	...	399	T.A.M. B.C. Vaccine	...	949
„ Dusart, 2 to 4 dr.	...	56	T.C.P.	...	73, 534
„ Eastoni, $\frac{1}{2}$ to 1 dr.	...	419	T.I.P.=Sod. Tet. iodo. phenol	...	phthalein.
„ „ Liq. pro., 9-18 m....	...	419	T.N.T.	...	316, 69
„ Eucalypti Gum $\frac{1}{2}$ -1 dr.	...	856	Tabaci Folia	...	873
„ Ferri Brom., $\frac{1}{2}$ to 1 dr.	...	417	Tabaiaco	...	625
„ „ et Quin. Cit., 1 dr.	...	726	Tabardillo	...	609
„ „ Iodidi, $\frac{1}{2}$ to 1 dr.	...	416, 79	TABELLÆ, Chocolate Tablets	...	804
„ „ Phosph., $\frac{1}{2}$ to 1 dr.	...	418	„ Antiasthm., 1 to 4 t.d.	...	578
„ „ Phosph. Co., $\frac{1}{2}$ to 2 dr.	...	418, 30	„ Antimonii Sulph.(0.01Gm.)	...	157
„ „ Phosph. c. Quin et Strych.('Easton'),	$\frac{1}{2}$ to 1 dr.	419	„ Apomorph., 1/100, 1/50 gr.	...	171
„ Ficorum, 1 to 4 dr.	...	401	„ Bism. et Pepsin. 3 gr.	...	230, 663
„ Formatum Co., 1-2 dr.	...	36	„ „ c. Cascara 1 gr	...	230
„ Glucosi	...	696	„ Caffeinæ Cit., 1 gr.	...	250
„ Glyceroph. Robin, 1 to 4 dr.	...	40	„ Cocainæ, 1/20 to $\frac{1}{2}$ gr.	...	339
„ „ Co., 1 to 2 dr.	...	40	„ Diacetyl Morph., 1/10 gr.	...	566
„ „ c. Format., 1 dr.	...	40	„ Digitalin, 1/10 gr., et Nitroglycerin, 1/100 gr.	...	400
„ Heroin, 1 to 2 dr.	...	566	„ Erythrol Nitratis, $\frac{1}{2}$, $\frac{1}{4}$, $\frac{1}{8}$, 1 gr., 1 or 2...	...	408
„ Hypoph., 2 dr.	...	692	„ Exalgin, $\frac{1}{2}$ gr.	...	3
„ „ Co., $\frac{1}{2}$ to 2 dr.	...	691	„ Glonoini, 1/100 gr.	...	577
„ „ Fellows', 1 to 2 dr.	...	692	„ Lecithin, $\frac{1}{2}$ gr.	...	540
„ Iodo-Tannic, $\frac{1}{2}$ -2 dr.	...	513	„ Mannitol Nit., 1 gr.	...	409
„ Ipecac.	...	525	„ Menthol, 1/5 gr.	...	558
„ Kolæ Co., 1 to 2 dr.	...	253	„ Nitroglycerini, 1/600, 1/400, 1/200, 1/100, 1/75, 1/50, 1/25 gr. and 1 mgr. 1 or 2	...	577
„ Lactucarii. av. 2 dr.	...	502	„ Nitroglyc., 1/100 gr. c.	...	578
„ Limonis, $\frac{1}{2}$ to 1 dr.	...	867, 881	„ Caffeine, 1 gr.	...	578
„ Mori, 1 dr.	...	871	„ Nitroglyc., Sod. Iod. c.	...	578
„ Neurotonique, 2 to 3 dr.	...	726	„ Arsen.	...	578
„ Parrish's $\frac{1}{2}$ to 2 dr.	...	418	„ {Nitroglyc. 1/150 to 1/100 } 578	...	
„ Picis Liq., 1 to 2 dr.	...	704	„ {Strych., 1/100 to 1/20 } 578	...	
„ „ c. Codeina, $\frac{1}{2}$ to 2 dr.	...	704	„ {Nitroglyc., 1/200 to 1/100 } 579	...	
„ Pilocarpin. et Pot. Brom., 1 dr. to 1 oz.	...	696	„ {Thyroid., $\frac{1}{2}$ to 3 gr. } 579	...	
„ Pini Pumil., 1 dr.	...	701	„ Nitroglyc. Co., 1 or 2	...	578
„ Pini Terpin et Heroin, 1 dr.	...	701	„ Papain, 2 gr.	...	652
„ Pruni Virg., $\frac{1}{2}$ to 1 dr.	...	879, 154	„ Pepsinæ, 3 gr.	...	663
„ Rami, acc. to age.	...	246	„ „ et Bismuth, 1 to 2	...	663
„ Rhamni, $\frac{1}{2}$ to 1 dr.	...	858	„ „ et Caffeine, 1 to 2...	...	663
„ Rhei., $\frac{1}{2}$ to 2 dr.	...	—	„ „ et Strychninæ	...	663
„ „ Aromat., av. 2 dr.	...	881	„ Phenolphthalein, $\frac{1}{2}$, 2 and 4 gr.	...	678
„ Rosæ, $\frac{1}{2}$ to 1 dr.	...	882	„ Phenolph., 4 gr., c. Ext.	...	678
„ Scillæ (& Co.), 30 to 60 m.	...	885	„ Rhei, 3 gr.	...	740
„ Senegæ, 1 dr.	...	886	„ Quin. Tannat., 1 gr.	...	740
„ Sennæ, $\frac{1}{2}$ to 2 dr.	...	886	„ Sodii Nitrits et Sodii Iodidi	...	776
„ Sulphatum, 4 dr.	...	261	„ Sodii Nitrits Co....	...	776
„ Tann-Iodo-phosph., $\frac{1}{2}$ to 2 dr.	...	514	„ Strophanthi Tinct., 1 m.	...	791
„ Thymi, 1 to 4 dr.	...	892			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME	DOSE	PAGE
Tabellæ—contd.			Tablets, Compressed—contd.		
„ Suprarenal Ext., $\frac{1}{2}$ gr. ...		976	Bismuth Pepsin and Char-		—
„ Trinitrini, 1-130 gr. ...		578	coal, 2 gr. each ...		—
TABLETS, COMPRESSED—TABLETTÆ			Blaud's Pill, 4 and 8 gr. ...		412
801. <i>In demand</i> are:—			„ „ 4 gr. c. Arsen., $\frac{1}{64}$ gr. ...		182
Acetanilide, 3 gr. ...		2	Bon Voyage		42
„ et c. Caffeine, 1 gr. ...		3	Boric Acid, 5 gr. ...		9
Aceto-Salicyl. Acid., 5, 8 gr.			Brain Ext., 5 gr. ...		959
(and with Phenacetin also			Brominol = 9 gr. Pot. Brom. ...		245
with Dover Pdr.) ...		76	Bromural, 5 gr. ...		821
Acid Lactic Bacilli, 3 to 6 p.d.		57	Butyl-Chloral c. Gelsem. ...		247
Aconiti = $2\frac{1}{2}$ m. Tincture ...		99	Caffeine, 1 gr. c. Antipyrin, 3 gr. ...		250
Acriflavine, 0.87 grain, and			„ Cit., 2 gr. ...		250
1.75 grains for Lotions ...		302	„ HBr., 2 gr. ...		250
Adalin, 5 gr. ...		820	„ „ 1 gr., c. Phenacetin,		
Adrenalin, $\frac{1}{200}$ gr.		981	4 gr. ...		250
„ $\frac{1}{300}$ gr., with Cocaine			Calc. Lact., 5 gr. ...		56
$\frac{1}{2}$ gr. ...		981	Calc. Sulph., $\frac{1}{2}$, $\frac{1}{2}$, 1 gr. ...		261
Alkagen, 1 to 3 ...		546	Calomel, $\frac{1}{10}$ to 5 gr. ...		474
Allonal, 1 to 2 ...		821	{ Camphor, $\frac{1}{2}$ gr. ... }		264
Aloes et Ferri, 4 gr. ...		137	{ Quin. Ac. Sulph., 1 gr. ... }		
Aloin, $\frac{1}{10}$ and $\frac{1}{2}$ gr. ...		138	Camph. Monobr., 1 gr. ...		265
„ Compound ...		138	Cannabis = 5 m. Tinct. ...		266
Alopon, $\frac{1}{2}$ gr.		632	Carbolic Acid, $\frac{1}{2}$, $\frac{1}{2}$ gr. ...		15
Alypin, $\frac{1}{2}$, $\frac{5}{6}$ and $3\frac{1}{2}$ gr. (and $\frac{1}{2}$			Cascara Ext., 1 to 5 gr. ...		279
c. Suprarenin) ...		345	Catha Ext., $2\frac{1}{2}$ gr. ...		847
Ammon. Brom., 5 and 10 gr. ...		144	Cerebral, 5 gr. ...		959
„ Chlor., 3 and 5 gr. ...		145	Chinosol, 5, 8, 15 gr. ...		317
„ „ 3 c. Borax, 2 gr. ...		145	Cinchonidine Sulph., 5 gr. ...		723
„ „ c. Glyc. Ext., 3 gr. ...		146	Choralamide, 5 gr. ...		284
„ Quinine and Comp. 738, ...		739	Chloramine T. ...		52
Anabolin, 1 to 3 ...		963	Chloral Hyd., 5 and 10 gr. ...		
Anticonstipation ...		138	(to be dissolved) ...		283
Antifebrin, 3 gr. (et c. Caf-			Codeine Phosph., $\frac{1}{2}$ and $\frac{1}{2}$ gr. ...		357
feine, 1 gr., 3) ...		2	Codeonal, $2\frac{1}{2}$ gr. ...		569
Antipyrine, $2\frac{1}{2}$ and 5 gr. (et			Colalin, $\frac{1}{2}$ and $\frac{1}{2}$ gr. ...		783
3 gr. c. Caffeine, 1 gr.) ...		329	„ Laxative, $1\frac{1}{2}$ gr. ...		783
Antiseptic (Thymol, etc.) ...			Col. Co. = 4 gr. pill. (B.P. '14)		
Antityphoid		779	Collargol, $\frac{1}{2}$ gr. ...		176
Apomorphine, $\frac{1}{100}$, $\frac{1}{50}$ gr. ...		171	Comp. Hypophosphites ...		692
Arsamin, 1 gr. ...		190	Cotarnin HCl., $\frac{1}{2}$ gr. ...		574
{ Arsenic, $\frac{1}{60}$ gr. ... }			„ Phthalate, $\frac{1}{2}$ gr. ...		574
{ Iron Hypoph., 2 gr. ... }		182	Corpus Luteum, 1 gr. ...		960
{ Quin. Ac. Sulph., 1 gr. ... }			Cystazol, 10 gr. ...		453
Arsenious Acid, $\frac{1}{100}$, $\frac{1}{50}$,			Cystoformin, 15 gr. ...		454
$\frac{1}{20}$ gr. ...		179	Dial, $1\frac{1}{2}$ gr. ...		821
„ $\frac{1}{64}$ gr., with Mer-			Didymin, 5 gr. ...		983
curic Chloride, $\frac{1}{64}$			Digitoxin, $\frac{1}{250}$ gr. ...		399
gr. ...		181	Dinner ...		708
Aspirin, 5 and 8 gr., and			Dormigene, 5 gr. ...		821
with Phenacetin, $2\frac{1}{2}$ gr., and		76	Dover's Powder, 5 gr. ...		525
with Dover's Pdr.		84	Duodenal Ext. = 5 gr. ...		960
Aspirodine, 5 gr. ...		317	Easton Syrup = $\frac{1}{2}$ & 1 dr. (&		
Atophan, 4 and 8 gr.		213	c. Arsen.) ...		420
Atrop. Sulph., $\frac{1}{100}$ gr. ...		572	<i>Effervescing, see 'Vescettes.'</i>		
Benzonaphthol, 5 gr. ...		447	Ephedrine HCl., $\frac{1}{2}$ gr. ...		855
Benzosol, 5 gr. ...		571	Ergotin, 1, 2 and 3 gr. ...		405
Betanaphthol 3 and 5 gr. ...		571	Ergotin, Senecin Co. ...		405
Betanaphthol, 5 grains, c.			Eserine and Trunczek's Serum ...		694
Phenolphthalein, 3 gr. ...		571	Eucaine- β , $\frac{1}{10}$ gr. ...		344
Bismuth Carb., 5 gr.		228	Euflavine 0.87 and 1.75 gr.		
„ Salicyl., 5 gr.		232	for lotions ...		306
„ Subnit., 5 and 10 gr.		235	Euflavine, $\frac{1}{2}$ and 1 gr. per os. ...		806
„ et Pepsin, aa 3 gr. ...		230	Euonymin, $\frac{1}{6}$ to 4 gr. ...		410
„ Pepsin & Cascara, t.d. ...		230	Exalgine, $\frac{1}{2}$ gr. ...		8

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE
Tablets—<i>contd.</i>		
Ext. Filicis, 3 m.	422
Fæxin Ext., 3 gr.	280
Felamine, 1 to 3	783
Ferri Arsenas, $\frac{1}{2}$ gr.	184
Ferri Bland c. Arsen. 1/64 gr.	182
Ferri Carb. Sacch., 5 gr.	412
„ Quin. Citr., 3 gr.	726
Formaldehyde Disinfectant	131
„ $\frac{1}{2}$ gr. c. Sacch. Lact., 2 gr.	132
Formamint	132
Gland ('Three' and 'Four'), 1 or 2	989
Glyceroph. Co.	40
Grey Powder, $\frac{1}{2}$ to 3 gr.	—
Grey Powder, 1 gr., and Dover's Powder, 1 gr.	—
Gualacol Benz., 5 gr.	447
„ Carb., 5 gr.	447
Gualac. & Sulph., <i>aa</i> 3 gr.	445
Hexamine, 5 gr.	452
„ & Lith. Benz.	453
„ Sod. Benz.	453
Hyd. Iodid. Flav., $\frac{1}{2}$ gr.	465
„ „ Vir., $\frac{1}{2}$ gr.	465
„ „ Rub. $\frac{3}{8}$ to $\frac{1}{2}$ gr.	462
„ Perchlor., 1/100, 1/32, 1/16 & 1/10 gr.	471
„ Subchlor., 1/10, $\frac{1}{8}$, $\frac{1}{4}$, $\frac{1}{2}$, 1, 2, 3, 4, and 5 gr.	474
Hydrastine Compound	493
Hypophos. Co.	692
Ichthosulphol, 2½ gr.	504
Insulin HCl. 10 units	643
Iodinol, 3 gr. of 25%	520
Iodoprotein, 5 and 10 gr.	522
Ipecac., 1/20, 1/10, $\frac{1}{4}$, 5 gr.	524
Iron Quin. Cit., 3 gr.	726
Kurchi Bark, 5 gr.	862
Lactobacilline	57
Lactobac-Glycogen	57
Laverain	742
Lecithin, 1½ gr.	540
Lithium Carb., 5 gr.	542
„ Citrate, 5 gr.	542
Livingstone Rousers	740
Luminal, $\frac{1}{2}$, $\frac{1}{4}$, 1, and 1½ gr.	822
Luminal-Sodium, 1 gr.	822
Lymphatic Gland	963
Magisal, 5 gr.	79
Magnes. Perox. 3 gr.	496
Malonurea, 5, 8, 10 gr.	817
Mammary Gland, 2 gr.	963
Marienbad	139
„ Salt, and Anti-obesity	780
Medinal, 1, 2½ and 5 gr.	820
Mesentery Gland, 5 gr.	963
Mixed Gland	989
Migralgin, 8 & 15 gr.	252
Mucin, 5 gr.	963
Myelin. 3 gr.	959
Nitroglycerin,—1/50 gr. ...	<i>Atis</i>	578
Sodi. Iodid., 15 gr. ...	<i>horis</i>	
Liq. Arsenical, 2 m.	

(See also Tabellæ 577 *et. seq.*)

NAME.	DOSE.	PAGE
Tablets—<i>contd.</i>		
Nitropropiol (Sugar Test)	377
Novocain with Adrenalin var.	346
Nuclein, 1 gr.	280
Omnopon, 1/6 gr.	632
Opium, $\frac{1}{2}$, 1 gr.	630
Orchitic Subst., 5 gr.	983
Ovarian, 5 gr.	963
Ox Bile 533; Stearettes, 5 gr.	411
Pancreatin and Soda	638
„ and Bile Salts	639
Papain, 2 and 5 gr.	652
Papaverine, $\frac{1}{2}$ gr., Hyoscy- amine 1/300 gr., and Benzyl Succ., 5 gr.	563
Paraform	131
Parathyroid, 1/20, 1/6, $\frac{1}{4}$, $\frac{1}{2}$ gr.	993
Pepsin, 3 gr.	663
„ 3 gr. et Caffeine, 2 gr.	663
Peptonic (Pepsin, Pancreatin, Calcium Lactoph., each 1 gr.)
Phenacetin, 4, 5 & 10 gr.	326
„ 4 gr., c. with Caff., 1 gr.	326
„ and Sulphonal 2½ gr. ea.	326
Phenalgin, 5 gr.	3
Phenoloid	32
Phenolphthalein, $\frac{1}{2}$, 2, 4 gr.	678
„ Comp.	678
Phenoquin, 4 and 8 gr.	317
Phenyl-Aspirodine, 5 gr.	89
Phenyl Sedasprin, 5 gr.	90
Pilocarpin Nit., 1/10, 1/5 gr.	695
Piperazine, 5 gr.	703
Pituitary Dried, 1 gr. entire gland	967
Planadalin, 5 gr.	820
Podoph., 1/4 to 1 gr.	707
Potass. Bicarb., 5 gr.	—
„ Brom., 5, 10 gr.	710
„ Chlor., 5 gr.	711
„ „ 3 gr., c. Ammon. Chlor. 1 gr., c. Borax, 2 gr. et c.	...	711
„ Borac. et Cocaina...	711
Pot. Iodide, 5 gr.	716
„ Permang., 1-5 gr.	555
„ Pot. Permang. & Alum for Water Purifn.	555
Proflavine, 0.87 and 1.75 gr. for lotions	306
Propional, 1½ gr.	820
Pulv. Cret. Arom. c. Op., 5 gr.	629
Quinidine Sulph., 5 gr.	722
Quin. Acetyl-Salicyl., 3 gr.	735
„ Ethyl-Carb., 8 gr.	742
„ HBr. 3 and 5 gr.	727
„ HBr. 3 gr. c. Phenac., 5 gr.	727
„ HCl., 1 to 5 gr.	728
„ „ Acid, 1, 3, 5 gr.	731
„ Rhei Co.	740
„ Salicyl., 3 gr.	735
„ Sulph., 1 to 5 gr.	737
„ „ Acid, $\frac{1}{2}$ to 5 gr.	739
„ „ Ac. 1 gr. c. Camph., $\frac{1}{2}$ gr.	264, 73

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Tablets—contd.			Tablets—contd.		
Quin. Sulph., Ac. 1 gr. Camph.			Thiocol, 5 gr.	448
1/5 gr. et c. Aconite Tinct., 1 m.		739	Three Gland	989
„ „ Camph., Morph.			Thyminic Acid, 4 gr.	...	984
et Atrop.	...	739	Thymoform	812
Red Bone Marrow, 3 gr.	...	958	Thymol Carb., 10 gr.	...	812
Regenerative, 6 <i>per diem</i>	...	769	Thymus Gland, 3 & 5 gr.	...	983
Rennet, 661; Rennin, 1 gr.	...	661	Thyroid (Standard), 1½ & 5 gr.	...	988
Resorcin, 3 gr.	...	751	„ Comp. (3 & 4 gland)	...	989
Rhubarb, Soda and Ginger...	...	881	Tinct. Aconit., 2½ m.	...	99
Saccharin, ½ gr.	...	755	„ Bellad., 2 & 5 m.	...	226
Salicin, 5 gr.	...	80	„ Cannab.=5 m....	...	266
Salipyrin, 5 gr.	...	329	„ Nuc. Vom., 5, 10 m.	...	599
Salol, 5 gr.	...	81	„ Opii, 5 & 10 m.	...	631
Salophen, 5 gr.	...	90	„ Quin. Ammon.=1 dr.	...	738
Santalol, 3 m.	...	623	„ „ „ Comp.	...	739
Santonin, 1, 2 & 3 gr.	...	760	„ Strophanth, 2 & 5 m.	...	791
Sedasprin, 5 gr.	...	85	Trilactine, 3 to 6 <i>p.d.</i>	...	57
Senecio Co.	...	886	„ Intestinal, 3 to 6 <i>p.d.</i>	...	57
Sidonal, New, 7½ gr. each	...	703	Trional, 5 gr....	...	796
Soda Mint (Sod. Bicarb., Am. Carb., & Mint).			Trivalin	...	826
<i>For Effervescing Compounds see 'Vescettes'</i>			Trunecek's Serum	...	768
Sodii Acid Sulph.	...	779	Tylcalsin, 8 gr.	...	77
„ Arsenat Co.	...	185	Tyllithin, 8 gr.	...	79
„ Benzoate, 2 gr.	...	8	Tylmarin, 5 gr.	...	28
„ Bicarb., 5 gr.	...	—	Urethane, 5 gr.	...	824
„ Bisulph. for Baths	...	779	Urotropine, 3, 5, & 7½ gr.; Eff., 5 gr.	...	452
„ Bromid., 5 gr.	...	770	Varium.	...	964
„ Chlor. et Borac.	...	773	Veramon, 1 to 1½ gr.	...	330
„ Citras, 5 & 10 gr.	586, 773		Veronal, 5, 8 and 10 gr.	...	817
„ Desoxychlorate.	...	784	Veronal Sodium, 1, 2½ & 5 gr.	...	820
„ Iodid c. Sodii Nitrite,			Vesalvine, 5 gr.	...	452
3 gr. with ½ gr., also			„ 'S' 5 gr.	...	453
5 gr. with 1 gr.	...	776	Water, Sterilising	45, 52, 779	
„ Nitris, 2½ gr. and Co.	775, 776		Yohimbine HCl., 1/13 gr.	...	895
„ Perborate Mouth	...	13	Zinc Oxide, 2 gr.	...	828
„ Salicyl., 3 & 5 gr.	...	70	TABLETS, HYPODERMIC	...	803
Solurol, 4 gr.	...	984	<i>Chiefly in demand are:—</i>		
Sonéryl, 1 gr.	...	821	Aconite Nit., 1/640 gr.	...	100
Spinal Cord, 2½ gr.	...	950	Adrenalin, 1/300 gr., c. Cocaine HCl., ¼ gr.	...	981
Stannoxyd	...	888	Apomorph. HCl., 1/20, 1/15, 1/10 gr.	...	171
Strontium Brom., 5 gr.	...	789	Atrop. Sulph., 1/200 to 1/50 gr.	...	214
Strophant. Tinct., 2 & 5 m.	...	791	Atrop. c. Morph.	...	214
Strych. Sulph., 1-60 to 1-30 gr.	...	794	Caffeine Sod. Salicyl., ½ gr.	...	251
Strych. c. Nitroglyc. (Tabellæ)	...	578	Cocaine Hyd., 1/10-½ gr.	...	338
Stypticin, ½ gr.	...	574	Codeine Phosph., ¼ and ½ gr.	...	357
Styptol, ¼ gr.	...	574	Curare, 1/12 gr.	...	853
Sulphonol, 5 gr.	...	795	Diamorph. HCl., 1/24, 1/12 gr.	...	566
Sulph. Præcip., 5 gr., c. Pot. Acid. Tart., 1 gr.	...	798	Digalen	...	400
Supra-renal, ½ & 1 gr. Dry Substance	...	975	Digitalin, 1/10 gr.	...	400
Syr. Easton=½ & 1 gr.	...	420	Ephedrine HCl., ½ gr.	...	855
Testicular Substance	...	983	Ergamine, 1/65 gr.	...	407
Thallium Acet., 0.1, 0.01 and 0.001 Gm.	...	891	Ergotinine Cit., 1/200 to 1/100 gr.	...	406
Theobromine Comp., up to 6 <i>p.d.</i>	...	806	Ergotoxine, 1/100 gr.	...	406
Theobrom. Sod. Format. 8 gr.	...	805	„ 1/100 c. Morph. ½	...	406
Theobrom. Sod. Salicyl, 5 gr.	...	806	„ 1/100 c. Strych., 1/20	...	406
Theocin Sod. Acet., 4 gr.	...	807	Heroin HCl., 1/24, 1/12 gr.	...	566
Theophylline, 4 gr.	...	807	Homatropine HBr., 1/200 gr.	...	217
			Hyd. Perchlor., 1/60, 1/50, & 1/30 gr.	...	471

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Tab. <i>Hypod.</i> — <i>contd.</i>			Targowla Reaction ...		584
Hyosine HBr., 1/400 to 1/75			<i>Tartar Emetic</i> ...		161
gr. ...		498	Diaphoretic, 1/24 to ½ gr.		
Hyosine Comp. ...		500	Emetic, ½ to 1 gr. ...		12
Hyoscyamine Sulph., 1/100,			Tartarus Boraxat, 20 to 40 gr.		238
1/50 gr. ...		503	Tartro Bismuthates ...		635
Lobeline Sulph., ⅞ gr. ...		544	Tatcho ...		1093
Morphine mec., ⅓ and ½ gr.		564	Tattoo Marks, to Remove ...		95
„ HCl., ½ to 1 gr. ...		563	Taurin ...		890
„ Hypophosph., ½, ⅓ & ¼			Taxine, 1/100 to 1/60 gr. ...		135
gr. ...		563	Tea, 248, 51; Tea Seed Oil ...		876
„ Sulph., ½ to 1 gr. ...		564	Teel Oil ...		930
„ c. Atropina ...		564	Teeth Infection... ..		843
„ c. Nitroglycerin ...		564	Teinture de Badiane ...		
Nitroglycerin, 1/100 & 1/250			Teinture de Camph. Conc. and		263
gr. ...		576	faible ...		
Novocain and Adrenalin ...		346	Teinture de Fève de Saint-		599
Physostig. Salicyl., 1/100 gr.		693	Ignace max. 4 m. ...		
Picrotoxin, 1/100 gr. ...		695	Teinture d'Iode Fr. Cx., 1908		515
Pilocarpine HCl., ½ gr. ...		695	and Supp. 514, ...		515
„ Nit., 1/10 to ½ gr. ...		727	„ „ Officinale ...		168
Quinine HBr., ½ gr. ...		731	Teintures var. <i>vide</i> Tinct. ...		168
„ HCl. Acid. 1, 2, 3 gr. ...		408	Telakucha ...		
Sclerotic Acid 1/16 gr.			Tellurium Organic Comps. ...		168
Scopolam. Morph. (and with			„ Spirochaeticide, Action		
Atrop.) ...		500	of Metal ...		261
Sparteine Sulph., ½ gr. ...		784	Temperature Indicators ...		841
Strophanthin, 1/500 gr. ...		791	Tenaline ...		270
Strychnine Nit., and Sulph.			Tensile Gloves ...		858
1/100 to 1/30 gr. ...		793, 794	Tephrosia ...		803
Tropacocaine HCl., 1/30 gr.		343	<i>Terebenum</i> , 5 to 15 m. ...		699
Tyramine ...		407	Terebinthina ...		168
Tablets, Ophthalmic. <i>Vide</i> La-			<i>Tereh. Canadensis</i> ...		890
melle.			„ Chia, 5 to 10 gr. ...		148
Tablet Triturates ...		803	Terebentene ...		855
Tabotamp ...		542	Terminalia ...		123
Tænia ...	422, 759, 1098		Terpeneless Oils ...		842
Taffetas Film ...		435	„ Oi. Aurant. ...		123
Taka-disatase, 1 to 5 gr. ...		551	Terpenes ...		804, 242
Talc (and Talc. Purif.) ...		144	Terpineol and Terpilanol ...		130
Tallquist Scale ...		394	Terpinoform ...		804
<i>Tamarind</i> , 1 to 8 dr. ...		890	Terpinol, 1 to 5 m. ...		
Tambach's Test ...		96	Terpine, Terpin. Hydrat., 2 to		
Tampons, Gauze ...	431, 801		6 gr. ...	804, 277, 242	
„ Argyrol, 5 & 10% ...		801	Terra Alba ...		143
„ Ichthosulphol ...		504	Terra Silicea Purificata ...		415
Tanacetum ...		890	Test, Breakfasts ...		982
Tannalbin, 8 to 15 gr. ...		95	Testiculin, 15 to 30 m. ...		982
Tannal Insolubile ...		95	Testis ...		983
Tannigen, 5 to 15 gr. ...		96	Testogan ...		
<i>Tannin</i> , 5 to 10 gr. ...		94	Tetanus Antitoxin, 931; Im-		
„ Albumin Test ...		364	munity Units, 933; Dried		
„ Tampons ...		801	Serum, 933; Mag. Sulph.		
Tannyl Acetate... ..		96	Injection, 547; Intracerebral,		
Tanret's Reagent ...		83	933; Preparation, 933;		
Tansy, 890; Tantalum, 168;			Quinine in relation 933;		
Tapioca Starch ...		839	Veterinary Use, 933; War		
Tapeworm ...	422, 759, 1098		Off. Memo, 932; Wound		
<i>Tar</i> , 2 to 10 gr. ...		703, 149	Dressing, 931, 932; Ana-		
Tar Acids, 30; Oils ...		30	Phyl. Shock, 932; Passive		933
Tar Spirit ...		704	Immunity ...		969
„ water ...		703	Tethelin ...		679
<i>Taraktogenos</i> ...		605	Tetiothalein Sodium ...		399
<i>Taraxacum</i> (30 to 120 gr.) ...		890	Tetrabromfluorescein ...		242
„ Cocoa, ½ oz. ...		890	Tetrabromphenolphthalein ...		

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Tetrachlorethane ...	293, 442,	59	Thigenol	505
Tetracholrethylene	293	Thio-carbamide	816
Tetra-ethyl lead... ..	659,	151	Thiocol, 15 gr.	448
Tetraform, 10 to 45 m.	274	Thiocyanogen Value	87
Tetraiodo-eosin	399	Thiodin	765
Tetra-iodofluorescein	138	Thiodotoxyl	766
Tetra-iodophenol-phthalein			Thiohistamine	800
Sodium ...	679, 146,	242	Thionin Solution	549
Tetra-iodo-pyrrol, 1 to 3 gr.	510,	242	Thio-Resorcin	752, 244
Tetramethyl diamino-triphenyl-			Thiosinamin, $\frac{1}{2}$ gr. inc. to 2 gr.		
carbinol	323	(and Mull.)	764, 244
Tetramethyl-diarsine	185	Thiosinamin, Eth. Iodide (Inj.),		
Tetranitro-methyl-aniline	307	3 gr.	765, 244
Tetra-oxy-phthalophenon	678	Thiostab	94
Tetra Vaccine	949	Thio-Urea	816
Tetryl	307	Thomassen's Method	713
Teucrium	890	Thomson's Vaccines	901
Texas Fever	191	“Thoriac”	808
Thalleioquin	725	Thorii Aceto Coumaras, 28;		
Thallium	891	Camphorat. 808; Camph-		
„ Acet. ...	891,	133	Sulphonas, Cinnam., 808;		
Thamnidium	498	Chloridum, 808; Glycero-		
Thaolaxine	836	phosphas, 808; Hydroxidum,		
Thebaicum (Opium)	625	Nitras, 808, 277; Ortho-Coum.,		
Thebaine HCl., $\frac{1}{2}$ to 1 gr., <i>per os</i> .	891		808; Lactas, 808; Oleas,		
Theine, 1 to 5 gr.	248	809; Oxidum, 807; Phthalas,		
Thelygan	983	808; Quinas, Salicyl, 809;		
<i>Theobrom Ol.</i> ; Pasta ...	804 &	163	Sodium-Acetate, 809; Sodio-		
Theobromine, 1 to 5 gr. 249, 805 &	163, 242		Citras, 293; Sulphas, 808;		
„ Aceto-Salicyl., 1 to 5 gr.	805,		Sulpho carb., etc.	809
„ Calc. Salicyl., 7 to 15 gr.	806		Thorium... ..	807 &	351
„ -Iodo-Sal., 2 to 10 gr. ...	806		„ Pads	808
„ Lith. Salicyl., 5 to 15 gr.	806		„ Table of Elements	352,	353
„ <i>Sodium-Sal.</i> , 10 to 20 gr.	805		Thoron	352
„ Sodio Acet., 10 to 15 gr.	805,		Thorn-Apple	787
„ Sodio Form., 8 to 15 gr.	805		Threadworm	759, 1098
„ Sodio Iod., 8 to 15 gr.	806		Three Gland Tabs.	989
Theocalcine, 7 to 15 gr. ...	806		Thresh's Reagent	49
Theocin, 3 to 6 gr. ...	807		Thrombin	76
„ Sodium Acetate, 2 to 4 gr.	807		Thromboplastin	959
Theominal	823	Trophleol	410
Theophylline, 3 to 6 gr. ...	807, 244		Thuja	892
„ Sod. Acet., 2 to 4 gr.	807, 244		Thus Americanum	699
Theo-Sodo-Form., 8 to 15 gr. ...	805		Thyme	892
Theo-Sodo-Sal., 10 to 20 gr. ...	805		Thymaglycine, 10 to 30 m.	811
Theo-Sodo-Acet., 10 to 15 gr.	805		Thymobenzene	164
Therapia Sterilans	40	Thymoform Tablets	812
'Therapeutic Coefficient'	302	<i>Thymol</i> , $\frac{1}{2}$ to 2 gr.; Anthel-		
Therapeutic Index	1029	mintic, 15 to 30 gr. 809, 6,		
„ Substances Act ...	1023		56, 167, 244		
„ Regulations, 1024;			„ Antiseptic power,	267, 277	
„ <i>re</i> Pituitary... ..	969		„ Blue ...	190, 394, 414, 416	
„ Sterilised Catgut added.			„ Carb., 5-15 gr. ...	424, 812	
—P.J. ii./29,319.			„ Disinfectant ...	810, 277	
Thermiol	26	„ Iodide = Aristol ...	509, 244	
Thermit	142	„ Sol. (Volckmann's)	...	812
Thermofuge	431	„ Sulphonephthalein	190, 394	
Thermolaine	436	414, 416		
Thermo-Isolators 141; for milk,	483		„ Wool & Gauze ...	438, 812	
Thermometric Equivs. Vol. I. xxxiv			Thymophthalein 190, 394, 414, 416		
Thermos Flasks, 141; Expts. 484			Thymotal, 5 to 15 gr.	812
Thieleman's Drops, av. 30 m. 383			Thymus Gland (Liq. Ext., $\frac{1}{2}$ -2		
			dr.), 3-10 gr.	983
			Thymus Vulgaris ...	809, 892	
			Thyro-glandin, 3 to 5 gr. ...	989	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Thyroid Gland	984 & 171	<i>Tinct. Buchu</i> , $\frac{1}{2}$ to 1 dr.	...	845
„ B.M.R.	992	„ <i>Cacti-Grandif.</i> , 2-10 m.	...	849
„ <i>Dry</i> , $\frac{1}{2}$ to 4 gr.	...	988	„ <i>Calendulæ Flor.</i> , 5 to 20 m.	...	845
„ „ Extract „	...	988	„ <i>Calumbæ</i> , $\frac{1}{2}$ to 1 dr.	...	845
„ in the Frölich Syndrome	...	990	„ <i>Camph. Co.</i> , 30-60 m.	...	630
„ Manganese Treatment	553	„ <i>Cannatis Ind.</i> , 5-15 m.	...	266
„ Obesity	990, 1078	„ <i>Cantharidini</i> , 2 to 5 m.	...	269
„ Overdose	985	„ <i>Capsici</i> , 5 to 15 m.	...	272
„ Para Gland	993	„ „ <i>Æther</i>	273
„ References	989	„ „ <i>Fortior</i> , 1 to 3 m.	...	273
„ Solution, 5-15 m.	...	987	„ <i>Cardam. & Co.</i> , $\frac{1}{2}$ to 1 dr.	...	846
„ Tablets Standardised, $1\frac{1}{2}$...	988	„ <i>Carminativa</i> , 2-10 m.	...	895
„ and 5 gr.	988	„ <i>Caryophylli</i> , 2 to 10 m.	...	847
„ Variation and Assay	172	„ <i>Cascara Sag.</i> , 10 to 60 m.	...	279
Thyroidectomised goat's milk	...	994	„ <i>Cascarillæ</i> , $\frac{1}{2}$ to 1 dr.	...	848
Thyroidectin, 5 gr.	...	994	„ <i>Castorei</i> , $\frac{1}{2}$ to 1 dr.	...	848
<i>Thyroideum Siccum</i> , $\frac{1}{2}$ -4 gr.	...	988	„ <i>Catechu</i> , $\frac{1}{2}$ to 1 dr.	...	848
Thyroxin	985, 174	„ <i>Chirata</i> , $\frac{1}{2}$ to 1 dr.	...	851
Thyroxin Tabs., 0.2, 0.4, 0.8	...	986	„ <i>Chlorof. Co.</i> , 5-60 m.	...	291
„ and 2 mgr.	986	„ „ et <i>Morph. B.P.</i> 85,	...	290
Tick Fever	585	„ „ 5 to 10 m.	...	290
Tidman's Salt	779	„ „ et <i>Morphinæ Co.</i> , 5	...	290
Tiki-Tiki, <i>see</i> Beri-Beri	...	596	„ „ to 15 m.	...	290
Tiliæ Flores, Tilleul	506	„ <i>Cimicifugæ</i> , 30-60 m.	...	851
Tillman's Dressing	437	„ <i>Cinchonæ and Co.</i> , $\frac{1}{2}$ to 1 dr.	...	297
Tin, Tin Oxide	888	„ <i>Cinnamomi</i> , $\frac{1}{2}$ to 1 dr.	...	298
<i>Tinct. Aconiti</i> , 2 to 5 m.	...	98, 20	„ „ <i>Co.</i> , 20 to 40 m.	...	298
„ „ (Fleming), 1 to 5 m.	...	99	„ <i>Cocci</i> , 5 to 15 m.	...	847
„ „ et <i>Iodi</i> 99,	...	513	„ <i>Colchici Sem.</i> , 5-15 m.	...	357
„ „ <i>Nepaul</i>	835	„ <i>Collinsoniæ</i> , $\frac{1}{2}$ -2 dr.	...	852
„ „ (Turnbulls)	99	„ <i>Colocynth</i> , 3-15 m.	...	381
„ <i>Actææ</i> , 30 to 60 m.	...	851	„ <i>Condurango</i> , $\frac{1}{2}$ to 1 oz.	...	852
„ <i>Adonis</i> , 10 to 30 m.	...	835	„ <i>Conii</i> , 30 to 60 m.	...	382
„ <i>Æsculi Hippoc.</i> , 10 m.	...	835	„ <i>Convallæ</i> , 5-20 m.	...	852
„ <i>Agarici</i> , 20 to 60 m.	...	836	„ <i>Coronillæ</i> , 30-60 m.	...	852
„ <i>Aloes</i> , $1\frac{1}{2}$ to 2 dr., or $\frac{1}{2}$ to	...	137	„ <i>Coto</i> , 10 to 30 m.	...	383
„ 1 dr. rep.	137	„ <i>Croci</i> , 5 to 15 m. (B.P.'98).	...	853
„ „ <i>Co.</i> , 1 to 2 dr.	...	138	„ <i>Cubebæ</i> , $\frac{1}{2}$ to 1 dr.	...	91
„ <i>Alstoniæ</i> , $\frac{1}{2}$ to 1 dr.	...	838	„ <i>Cudbear</i>	396
„ <i>Amara. P.G.</i>	859	„ <i>Digitatis</i> , 5 to 15 m.	...	396 & 72
„ <i>Ananassæ Sativæ</i> , 30 m.	...	840	„ „ Assay of	...	396 & 73, 75
„ <i>Anodyna</i> , 5 to 30 m.	...	631	„ „ <i>Fol. Recent.</i> , 5 to	...	398
„ <i>Anthemidis</i> , 3-10 m.	...	840	„ „ 15 m.	...	398
„ <i>Anthoxanthi</i> , 2-6 m.	...	841	„ „ Keeping Properties	...	397 & 73
„ <i>Anticholerica</i>	383	„ „ of	...	397 & 73
„ „ <i>Inosemzowi</i>	383	„ „ <i>Phys. Standardised</i>	...	396 & 73, 75
„ „ <i>Thielemani</i> , av. 30 m.	...	383	„ „ <i>Sem.</i>	75
„ <i>Antiperiodica</i> , 1-4 dr.	...	739	„ <i>Droseræ</i> , 5 to 10 m.	...	854
„ <i>Apis</i> , 1 m. hourly	...	841	„ <i>Elaterii Co.</i> , 10 to 30 m.	...	855
„ <i>Apocyni Can.</i> , 5 to 60 m.	...	170	„ <i>Ergotæ</i> , 5 to 30 m.	...	405
„ <i>Arnica</i> , $\frac{1}{2}$ to 1 dr.	...	841	„ „ <i>Amm.</i> , 30 to 60 m.	...	405
„ „ <i>Flor.</i> , $\frac{1}{2}$ to 1 dr.	...	841	„ <i>Erythroph.</i> , 5 to 10 m.	...	409
„ <i>Aromatica</i>	852	„ <i>Eucalypti Fol.</i> , 15 to 120	...	856
„ <i>Asajetida</i> , $\frac{1}{2}$ to 1 dr.	...	842	„ „ 615; Gum, 20 to	...	410
„ <i>Asclepias var.</i>	842	„ „ 40 m.	...	856
„ <i>Aurantii</i> , $\frac{1}{2}$ to 1 dr.	...	842	„ <i>Euonymi</i> , 10 to 40 m.	...	410
„ <i>Avenæ</i> , 20 m.	...	842	„ <i>Euphorb. Pepli.</i> 30 to 60	...	857
„ <i>Baptisiæ</i> , 5 to 30 m.	...	843	„ „ <i>in die</i>	857
„ <i>Bellad.</i> , 5 to 15 m.	...	226	„ <i>Euphorb. Pil.</i> , 10 to 30 m.	...	414
„ <i>Benzoini</i> , <i>Co.</i> , $\frac{1}{2}$ to 1 dr.	...	6, 3	„ <i>Ferri Perchlor.</i> , 5 to 15 m.	...	416
„ „ <i>Simp.</i>	7	„ „ <i>Pomat.</i> , 15 to 30 m.	...	421
„ <i>Berberid.</i> , $\frac{1}{2}$ to 1 dr.	...	844	„ „ <i>Tart.</i>	—
„ <i>Blepharis</i> , 15 m.	...	844	„ <i>Gallæ</i> , $\frac{1}{2}$ to 2 dr.	...	848
„ <i>Boldoæ</i> , 10 to 20 m.	...	844	„ <i>Gambir Co.</i> , 1 dr.	...	848
„ <i>Bryoniæ</i> , 1 to 10 m.	...	845			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
<i>Tinct. Gelsemii</i> , 5 to 15 m. ...		428	<i>Tinct. Podoph.</i> Amm., 10-20m. ...		708
" <i>Gent. Amar.</i> ...		859	" <i>Pruni Virg.</i> , 30 to 60 m. ...		879
" <i>Gent. Co.</i> , $\frac{1}{2}$ -1 dr. ...		—	" <i>Pulsatilla</i> , 5 to 30 m. ...		879
" <i>Gossypii Rad.</i> , 1 dr. ...		443	" <i>Pyrethri</i> (& Co.)... ...		880
" <i>Guaiaci</i> , 1 in 10, 60 m. ...		445	" <i>Quassia</i> , 30 to 60 m. ...		880
" " <i>Ammon.</i> 30 to 60 m. ...		445	" <i>Quebracho</i> , 30 to 60 m....		881
" <i>Guaranæ</i> , 30 to 60 m. ...		861	" <i>Quillaia</i> , 30 to 60 m. ...		881
" <i>Hæmostyptica</i> , 5 to 30 m. ...		405	" <i>Quinina</i> , 30 to 60 m. ...		729
" <i>Hamam</i> , 30 to 60 m. ...		449	" <i>Quinina Am.</i> , 30 to 60 m. ...		738
" <i>Hydrastis</i> , 30 to 60 m. ...		493	" Loss of Ammonia in.—J. Rae, P.J. ii./29,310.		
" <i>Hyoscy.</i> 30 to 60 m. ...		501	" <i>Rhei Co.</i> , 2 to 4 dr.; $\frac{1}{2}$ -1 dr. rep.... ...		881
" <i>Ignatiæ</i> , 3 to 20 m. ...		599	" " <i>Amara</i> , $\frac{1}{2}$ to 2 dr. ...		883
" <i>Iodi Fortis</i> ...		514	" <i>Rhei Aromat.</i> , av. 60 m. ...		881
" " <i>Churchill</i> ...		516	" <i>Rhois</i> , 2 to 15 m. ...		882
" <i>Fr. Cx.</i> 1908 (<i>Sine Pot.</i> <i>Iod.</i>) 4 $\frac{1}{2}$ to 18 m. ...		514	" <i>Rumicis</i> , 1 to 10 m. ...		883
" <i>Iodi</i> " <i>Indian</i> " ...		514	" <i>Sanguinaria</i> , av. 15 m....		884
" <i>Iodinei</i> , Ed. ...		515	" <i>Scilla</i> , 5 to 15 m. ...		885
" <i>Iodi Mitis</i> , 2 to 5 m. 514 <i>et seq.</i>			" " <i>Phys. Std.</i> , 5 to 15 m. ...		885
" " <i>et Aconiti</i> ...		513			74, 75
" " <i>Æther</i> , 516; <i>Decol.</i> and <i>Decol. Fortis</i> , 516; <i>Oleosa</i> ...		516	" <i>Senecionis</i> , 1 to 2 dr. ...		886
" <i>Ipecac.</i> , 10 m. ...		525	" <i>Senega</i> , 30 to 60 m. ...		886
" <i>Iridis</i> , 30 to 60 m. ...		864	" <i>Sennæ Co.</i> (<i>Legum</i> , 886), 2 to 4 dr.; $\frac{1}{2}$ —1 dr. rep. ...		886
" <i>Ixoræ</i> , 1 to 1 $\frac{1}{2}$ dr. ...		864	" <i>Serpentaria</i> , 30 to 60 m. ...		887
" <i>Jaborandi</i> , 30 to 60 m....		696	" <i>Stramonii</i> , 5 to 15 m. ...		788
" <i>Jalapæ (et Co.)</i> , 30 to 60 m. ...		864	" <i>Strophanthi</i> , 2 to 5 m. ...		791
" <i>Kaladana</i> , $\frac{1}{2}$ to 1 dr. ...		865	" <i>Strophanthi Phys. Standard</i> 791 & 74, 161		
" <i>Kino</i> , 30 to 60 m. ...		866	" " <i>Fraser's</i> ...		791
" <i>Kolæ</i> , 20 to 60 m. ...		252	" <i>Sumbul</i> , 30 to 60 m. ...		889
" <i>Krameria</i> , 30 to 60 m. ...		866	" <i>Sydenham's</i> , 5 to 20 m....		631
" <i>Lachnanthis</i> , 1 to 10 m. ...		866	" <i>Thebalaica</i> , 20 to 30 m....		630
" <i>Lactucarii</i> , av. 30 m. ...		502	" <i>Thuja</i> , 2 to 5 m. ...		892
" <i>Laricis</i> , 20 to 30 m. ...		—	" <i>Tolutana</i> , 30 to 60 m. ...		843
" <i>Lasiosiphon</i> , 10 to 60 m. ...		867	" <i>Urgineæ</i> , 5 to 15 m. ...		892
" <i>Lavand. Co.</i> , 30 to 60 m. ...		—	" <i>Valeriana</i> , av. 1 dr. ...		825
" <i>Laxativa</i> , 20 to 60 m. ...		279	" " <i>Ammon. (et Indic.)</i> , $\frac{1}{2}$ to 1 dr. ...		825
" <i>Limonis</i> , 30 to 60 m. ...		867	" <i>Veratri Viridis</i> , 5 to 15 m. ...		893
" <i>Lobelia</i> , 15 m. expt., 60 m. emetic ...		544	" <i>Verbasci</i> , 20 to 60 m. ...		893
" <i>Lobelia Æther.</i> 5 to 15 m. ...		544	" <i>Viburn. Prunif.</i> , 2 to 4 dr. ...		894
" <i>Lupuli</i> , 30 to 60 m. ...		868	" <i>Warburgii</i> , 1 to 4 dr. ...		739
" <i>Lycopodii</i> , 15 to 60 m....		868	" <i>Zedoari</i> , 30 to 120 m. ...		739
" <i>Menthol Æther</i> ...		558	" <i>Zingib.</i> , 30 to 60 m. ...		895
" <i>Monsonia</i> , 1 to 4 dr. ...		871	" " <i>Fort.</i> , 5 to 20 m. ...		895
" <i>Moschi</i> , U.S., av. 1 dr. ...		871	<i>Tincturæ</i> , 812; <i>Dispensing of</i> " <i>Stabilised (Valerian)</i> , 824; " <i>Horse Chestnut</i> ...		813 824, 836
" <i>Myrrha</i> , 30 to 60 m. ...		872	<i>Tincture of Life</i> ...		811
" " <i>et Boracis</i> ...		872	<i>Tinctures</i> , <i>Aqueous</i> , <i>Glycerin</i> ...		812
" <i>Nucis Vom.</i> , 5 to 15 m. ...		599	" <i>Ethereal</i> , 812; <i>see Tinct.</i> " <i>Capsici</i> = <i>Æther</i> , etc. " <i>Isopropyl</i> ...		124
" <i>Opii</i> , 20 to 30 m.; 5 to 15 m. rep. ...		630	<i>Tinea</i> 569 & <i>Therap. Index</i> ...		765
" " <i>Ammon.</i> , 30 to 60 m. ...		631	<i>Tiodine (injection, 3 gr.)</i> ...		506
" " <i>Benz.</i> , $\frac{1}{4}$ -1 dr. ...		630	<i>Tiqui Tiqui</i> , ...		506
" " <i>Camph.</i> , av. 1 dr. ...		630	<i>Tisane de Polygala</i> , 886; various		506
" " <i>Crocata</i> , 5 to 20 m. ...		631	<i>Titanium</i> , <i>Chloride</i> , <i>Oxide</i> , " <i>Sulphate</i> , <i>Ferrocyanide</i> ...		58, 351
" " <i>Deod.</i> av. 8 m. ...		630	<i>Toad Flax</i> ...		837
" <i>Passiflora</i> , 30 m....		876	<i>Tobacco</i> , 873, 166; <i>Denicotinised</i>		874
" <i>Persionis</i> ...		91	<i>Toison's Solution</i> ...		396
" <i>Phosphori Co.</i> , 3 to 12 m. ...		690			
" <i>Phyostig.</i> , 5 to 15 m. ...		693			
" <i>Phytolac</i> , 3 to 10 m. ...		877			
" <i>Picrophiza</i> , $\frac{1}{2}$ to 1 dr. ...		877			
" <i>Podophylli (et Indic.)</i> , 5 to 15 m. ...		708			

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Todaiwo	881	Tri-iodomethane	507
Tolu	843	Tri-iodophenol	21
Toluene Sodium Sulphone Chlor- amide	51	Trikresol34, 264, 278	
„ Sulphone Chloride	51	„ Formalin	34
„ Sulpho-dichloramide	52	Trilactine Milk	58
Toluidine, 303; Toluidine Blue	535	„ Tablets, 3 to 6 p.d.	57
Toluol	312, 60, 244, 278		„ „ Intestinal	57
Toluol-azo-toluol-azo--B.Naph thol	13	Trillet's Method	366
Tolysin, 10 to 15 gr.	819	Tri-methanal Allyl Carbide	131
Tomb's Mixture	1046	Trimethyl-Vinyl-Amm. Hyd.	5
Tonquin Bean	29	Trimethylamine	870
Tonquinol	316	Trimethyl Benzene	541
Tooth Extraction	337	Trimethyl-Benzoxypiperidine, 1/10 to ½ gr.	844
„ Paste, 'Formosyl'	130	Trimethyl-Glycocoll	5
„ Pastes, Antiseptic Power	278	Trimine, 8 to 15 m.	552
„ Pdr., Jungman's, 888;		Trinitrin, 1/200 to 1/10 gr.	575
„ Sodium Perborate	13	„ Solution, ½ to 2 m.	576
Torbenite	355	„ Tabellæ, 1/130 gr.	577
Touch Wood, 838; Tow	487	Trinitrobenzol	311
Tournesol	92	Trinitrocellulose	359
Towels, 437; Sanitary, 436; Moss	786	Trinitroglycerin, 1/200 to 1/10gr.	575
Towle's Pills	635	Trinitrophenol	62
Town's Specific	226	Trinitro-Butyl-Toluene	316, 871	
Toxicophlœa, 835; Toxins, 896 <i>et seq.</i>		Trinitrotoluene	316, 60	
Toxol	34	Triolein, Palmitin, Stearin	158
Trachylobium	869	Trional, 10 to 20 gr.	796, 244	
Trade Marks, 1027; 'Avoided,'	1028		Trioxymethylene	131
„ „ for Patented Articles	1027		Tripanblue	191
„ „ Act (1919)	1028		Triple Valerianate Injection	826
Tragarantha, 2 to 10 gr.	813	Triticum...	837, 839	
Tragopogon	892	Triturations	814
Transfusion, Flood	995	„ Acidl Arsen., 1/6 to ½ gr.	
„ Solutions for	1, 767		„ Atropinæ Sulph., 1/20 to 1/10 gr.	
Traumatic Balsam, ½ to 1 dr.	6	„ Cocainæ HCl., ½ to 5 gr.	
Traumaticin	295	„ Ferri Arsenatis, ½ to 2½ gr.	
Trench Fever	586	„ Morphinæ HCl., 1 to 3 gr.	
Trepol	242	„ Pierotoxini, 1/10 to 2/5 gr.	
Treponema Pallid	196 &	574	„ Sodli Arsenatis, ½ to 1 gr.	
„ pertenuæ	612	„ Strophanthl (1 grain=10 m. Tinct. B. P. '14), 1/5 to ½ gr.	
„ recurrentis	569	„ Strychninæ, ½ to ¾ gr.	
Tribondeau's Stains	578	Trivalin hypod., 8 to 15 m; <i>per</i> <i>os</i> 8 m.	826	
Tribromophenol, ½ to 2 gr.	20, 4,	244	Trivalin c. Hyos. Valer.	826	
„ Bismuth, 5 to 20 gr.	20	Trochisci (Medicated Lozenges), F. with Fruit Paste, G. with gum basis i.e., 'Pas- tills' or 'Jujubes'; S. with sugar, R. with Rose, T. with Tolu.—Bases	814	
Tribromethylalcohol	246	Acidil Benzoici, ½ gr., F. and 1½ gr. (Stimulant Voice), T.H. ½ gr.	7	
Tribrom-Tert.-Butyl. Alcohol...	246	„ Benzoici Co. T. H. (Ben- zoic Acid, Codeine, Co- caine, Ipecac., Menthol & Red Gum (marked C.B.A.) „ Carbolici, 1 gr., (S.) (marked C.A.)	18	
Trichlorbutyl-Glycol, 5 to 20 gr.	247	„ Tannici, T., ½ gr. and G., „ Tannici, F., 1½ gr., T.H. „ Tannici et Capsici, F.		
Trichlorethyl-Glycol, 5 to 20 gr.	282			
Trichlorethylene	292			
Trichlor-isopropyl Alcohol	294			
Trichloromethane, 1 to 5 m.	284			
Trichlorophenol	21			
Trichlorophenyl-iodo-meth. Sal.	73			
Trichlor-Tert.-Butyl-Alc., 5 gr.	248			
Trichomonas	543			
Tricocephalus	1098,	505			
Tricophyton	570			
Tricresyl Phosphate	442			
Triferrin, 15gr. p.d.	415			
Trifolia	870			
Trigemin, 12 gr.	330			
Trigonella	857			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Trochisci— <i>contd.</i>			Trochisci— <i>contd.</i>		
Aconiti, F., Tinct. $\frac{1}{2}$ m.	1		Nitroglycerini, <i>vide</i> Tabellæ.		
every $\frac{1}{2}$ hour	99	Opii, S., Ext. 1/10 gr., 2 to 6		
Adrenalin, 1/1000 gr.	982	<i>p.d.</i>	631
Althææ (Guimauve) <i>ad. lib.</i>			Orthoform, 2 gr., T.H. ...		652
Ammonii Bromidi, 1 gr. (G.)	145		Papain, $\frac{1}{2}$ gr., S., and 1/5 gr.		
Ammon. Chlor., F. 2 gr. ...	146		„ 1/5 gr., c. Cocaina, 1/10		
„ „ c. Glycyrrh., 3 gr. ...	146		gr., S.	652
Ammon. Chlor. Co. ...	146		Paregoric, S., 2 to 6 <i>p.d.</i>		
Antacidi (Sir W. Roberts)			Potassii Chloratis, R., 3 gr.,		
Calcii Carb., $3\frac{1}{2}$ gr.			also F., 3 gr., T.H....	711	
Mag. Carb., $2\frac{1}{2}$ gr.			„ et Boracis, $1\frac{1}{2}$ gr. ...		
Sodii Chlor., 1 gr.			„ Chlor. et Glyc. G., 3 gr.		
Bismuthi Co., R., 2 gr.		<i>p.r.n.</i>		
Boracis, F., 3 gr. T.H.			„ Nitratis, S., 3 gr., 3 to 6		
Boracis et Potass. Chlor., F.			<i>p.d.</i>	
Brompton Blacks ...	860		„ Tart. Acidi, F., 3 gr.		
Camphoræ, 2 gr., S., <i>p.r.n.</i> ...	264		Pyrethri, F., 1 gr., 3 to 6 <i>p.d.</i>		
„ Salicyl. Comp. <i>t.d.</i> ...	265		Rhei, Zingib. et Cardam ...		
Capsici, S., <i>p.r.n.</i>		Rose, S., <i>ad libitum.</i>		
Carbonis, S., 12 gr., 1 or 2 <i>p.c.</i>			Santonini, S., 1 gr., <i>h.s.</i> ...	760	
Cascara gr., $2\frac{1}{2}$ c. Menth. Pip.			Sedativi, F., 3 to 6 <i>p.d.</i> ...	631	
F., 1 or 2 ...	279		Sodii Bicarb., R., 3 gr., <i>p.c.</i>		
Catechu. 1 gr., F., 2 gr. T.H.	848		Sodii et Zingib., S., <i>p.c.</i>		
Chlorodyne, 4 m., S., '85.			„ Chlorat., 3 gr., 3 to 6 <i>p.d.</i>	773	
Cocain. HCl. S., 1/12 gr., T.H.			Sulphuris, 4 gr., 1 to 6 <i>p.d.</i> ...	798	
F., 1/10 (marked H.C.), G.			Terebene, 1 m., S.	
1/10, Brompt. $\frac{1}{2}$...	339		Tolutani S.		
Codein, $\frac{1}{2}$ gr., S., 4 or 5 <i>p.d.</i>	356		Tussis, 4 or 5 <i>p.d.</i> ...	525	
Cubebæ, F., $\frac{1}{2}$ gr., T.H. ...	853		„ Brompton ...	860	
Digestive (Rhei, Zing., Cardam)			Zingib., S., <i>ad lib.</i>		
Eucalypti Gum, F. 1 gr. ...	856		Trommer's Test ...	376	
Eucalypti Co., F., 1 gr. ...	857		Tropacocaine HCl. ...	343, 244	
„ Ol. 1 m. G.		Tropical Ulcer ...	552	
Ferri Redacti, S., 1 gr. 1 or 2	411		Tropæolin ...	418	
Formosyl (G.) ...	130		Tropic Acids Comps. ...	210	
Gambir, 1 gr.—Catechu		Tropyl Tropate... ..	210	
Glycyrrhizæ (et Anisi) ...	860		Truncck's Serum ...	768	
„ et Opii, $\frac{1}{2}$ gr.		„ with Eserine ...	694	
Gualiaci, 2 gr., T.H.F., and			Trotyl ...	316, 60	
S. Resinæ, F., 3 gr. ...	445		Trypaflavine ...	300	
Gummi Rub. c. Cocaina 1/20 (G.)			Trypagar ...	532, 536	
Hyd. Subchlor. S., $\frac{1}{2}$, 1, 2 gr.			Trypanosoma Gambiense char-		
Ipecac., S., $\frac{1}{2}$ gr., also F., 1 gr.,			acters ...	591	
2 or 3 <i>p.d.</i> ...	525		Trypanosomes <i>var.</i> ...	586 et seq.	
Kino, F., 2 gr., 1 <i>p.r.n.</i> ...	866		Trypanosomiasis, 190, Therap Ind. &		
„ Eucalypti, 1 gr., F. ...	856		586		
Krameria, 2 gr. et Cocaine,			„ Internat. Conf. 1925 ...	583	
1-10 gr. G., <i>p.r.n.</i>		„ Commission ...	589	
Krameria, F., Ext., 1 gr., G.			Trypan Blue and Red ...	190, 191	
2 gr., F. (T.H.), 3 gr., et Co-			Tryparsamide, 1 to 2 Gm.,		
cainæ, 1/20 gr., F....	866		injected weekly	209, 587, 593	
Lavandulæ, S., <i>ad lib.</i>		Trypsin ...	637, 639, 76, 143	
Magnesia, 5 gr., S., 2-4 <i>p.d.</i>			„ Broth ...	532	
Menth. Pip. (et Fort.).			„ in Fæces ...	413	
Menthol, S., $\frac{1}{2}$ G., 1/20, 1/10,			„ Stearettes ...	639	
$\frac{1}{2}$, $\frac{1}{4}$ gr.		Trypsinised Bl. Egg Med. ...	620	
„ 1/20, and Cocaine, 1/20			Tryptic Broth ...	606	
gr., G.		Tryptophane Reaction ...	411	
„ $\frac{1}{2}$, and Eucalyp., 1 m., G.			Tse Tse Fly ...	586	
Morphinæ, T., 1/32 gr., 4 or 5 <i>p.d.</i>			Tubache's Method ...	328	
„ 1/32 gr., et Ipecac., 1/10 gr.			Tubercle Bacillus	934 & 593	
T., 4 or 5 <i>p.d.</i> ...	563		Tubercle—Immune Cattle	595	
„ 1/40 gr., & Emetin, 1/80			„ Vaccines .	938	
gr. S., 4 or 5 <i>p.d.</i> ...	525		Tuberculin	936	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Tuberculin 'A.F.'	938	Tuberculosis, Infectivity of	594
„ Auto-inoculation	943	„ Lipase Treatment	763
„ B.C.G.	944	„ and Milk 935 & 487, <i>et seq.</i>	...	595, <i>et seq.</i>
„ 'B.E.,' (Human, Bovine	„ Notification Order	934
or mixed), 939; Dose	„ Order 1925 (cows)	934
Table	940	„ (See also Milk)
„ Beraneck's	945	„ Redhair, and in Wales	935
„ Bouillon Filtrate	938	„ Progress Infection, Dixon	...	934
„ Calmette Test	947	„ Proph. Vaccn. of new born	...	944
„ by Mouth	939	Tubes Témoins	261
„ Cross Vaccination	939	Tucker's Asthma Cure...	636
„ Cuti-reaction	947	Tung Oil	867
„ Diagnostic	946	Tungsten 315; Arc Light	315
„ Dispensaries ...	944, 597	...	Turck's Bottle and Capsule	414
„ Dose, Table ...	938, 940	...	Turf Moss	785
„ Dreyer's	942	Turnera <i>var.</i>	854
„ 'For and Against'	943	Turkey Red Oil	621
„ I K'	945	Turmeric	199
„ Intradermic Test	947	Turnbull's Tinct. Aconiti	99
„ Koch P.G. 'Old'	936	Turnsole...	92
„ Lundie's	946	Turpentine	699, 148	...
„ Mantoux Test	947	„ Injections in Arth-
„ Moro's Test	947	ritis, 675; in
„ Nathan Raw	941	Skin Affns., 700;
„ New (T.R.)	938	Punch	700
„ Ointment (Moro's)	937	Turpeth Minl.	476
„ (Philip)	947	Turpethum, 5 to 20 gr.	—
„ Old, 936; Standardisa-	Tutocaine	354
tion, 937; Diagnost.	Twilight Sleep	499
& Treatment	937	Tyalsin, 5 to 15 gr., Tablets,
„ Ophthalmic Reaction	947	8 gr.	77, 16, 246	...
„ Original Alt	938	„ Intrav. $\frac{1}{2}$ to 1 Gm.	78
„ Percutaneous Test	947	Tyllithin, 5 to 15 gr.	79, 246
„ Perlsucht, B.E. =	Tylmarin, 5 to 10 gr. (Tabs. and
Bovine B.E.	939	Cachets, 5 gr.) ...	28, 246	...
„ P.T.=Tuberculin Old	„ Dusting Pdr.; Gauze	28
(Bovine)	—	„ Quinine, 3 to 5 gr.	28
„ P.T.O.	938	„ Sodium, 5 gr.	28
„ P.T.R.=T.R.Bovine	939	„ Thorium	28
„ Raw's	941	Tylnatrin, 5 to 15 gr. ...	79, 16	...
„ Reactions Diagnostic...	946	Tylophoræ Fol, I.C. Add., $\frac{1}{2}$ to 2gr.
„ "R" (Raw's)	941	Tyndall Effect	365
„ References, Genl.	942	Typhoid 948, 996, 1095 & 603
„ Spahlinger's	946	„ Agglutinating Sera	604
„ Spengler's	945	„ Anti, Tablets	779
„ T.O.A.	938	„ Atropine diagnostic	604
„ Tables	938, 940	...	„ Bacillus	948 & 603	...
„ Tested Milk	471	„ Carriers	607
„ Tests	946	„ Vaccines	949
„ T.R.	938	„ Widal's Test	603
„ T.R. Dose Table	938	Typhol	34
„ „ <i>per os</i>	939	Typhus Fever	996 & 609	...
„ Von Pirquet Reaction	...	947	Tyramine, $\frac{1}{2}$ to $\frac{1}{4}$ gr. hyp.	...	407
Tuberculosis, 934, 593; and Flies	...	935	Tyrode's Solution	767
„ And Rainy Winds	597	Tyrosin	95, 365	...
„ Aetiology	935	Tyrotaxon	502
„ Austral. Quarantine	934	Uffelmann's Test	416
„ Auto-inoculation in	943	Ulexine, 1-20 to 1-5 gr.	854
„ Complement Fixation in	...	632	Ulmus <i>var.</i>	892
„ Death Rate	935	Ultra Violet Rays	315
„ in Dogs	597	„ „ Acetone Blue Gauge 317, 318
„ Graduated labour in	943	„ „ Alphabetical List of	...	319
„ Hospitals for Treatment	...	935	„ „ affections treated
„ Immunising Vaccine			
„ Raw	940			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Ultra Violet Apparatus	...	317	Ung. Brooke's	...	602
" " Comparison with Cod	...		" Cadmii Iodidi, 1 in 8	...	45
" " Liver Oil	...	317	" Calcis Chlorinat	...	834
" " Cut down by smoke	...	317	" " Iodat	...	834
" " Effect on skin	316, 317		" Calomel c. Morph. L.I.P.	...	475
" " General Notes on treatment	...	318	" Cantharidin c. Hyd. Co.	...	269
" " Germicidal effect of	...	316	" Cantharidini	...	269
" " Glass for	...	318	" Capsici, and Oleo-res.	272, 273	
" " Lamps, sale of	...	318	" Caseinæ	...	590
" " Method of use	...	317	" Castellani...	752 & 1051	
" " Penetrating Power	...	316	" Cedri Atlant	...	849
" " " and Rickets	...	596	" Cetacei, 1 in 5	...	849
" " Sugarsynthesis by aid of	320		" Chaulmoogræ	...	607
" " Water sterilisation by	316, 433		" Chrysarobini (& Co. 295)	...	294
" " Wave Lengths	...	316	" Cinereum	...	475
Ultramicroscope	...	576	" Citrine	...	466
Umbrenal	...	543	" Cocainæ, 4%	...	335
Uncinariasis, <i>see</i> Ankylostom.			" Conil.	...	382
Undulant Fever	...	559	" Crédé	...	176
Unguenta	...	815, 243	" Creolin Comp.	...	32
Unguentum, U.S.X. — Cera			" Creosoti, 1 in 10; Forte	...	385
Flav. 1; Adeps Benz., 4			" Cucumeris	...	853
Ung. Acid Borici, 1, 2, 3 (Martindale)	11	" Cupri Cit.	...	389
" " Carbol., 3%	...	18, 4	" " Oleat	...	601
" " " Co.	...	466	" Cyllin Comp.	...	32
" " " c. Cocaine	...	18	" " Danish	...	799
" " " Hyd. Perch.	...	19	" Demulcens	...	11
" " " Menthol	...	19	" Dermatol	...	237
" " Pheno-Borici.	...	11	" Desinficiens	...	471
" " Picrici, 1 to 3%	...	63	" Deeks (Dhobie's Itch)	...	1051
" " Salicyl, 2%	66	" Diachyli	...	603
" " " Terebinth	...	73	" " Carbol.	...	608
" " " Co.	...	67	" Eth. Hyd. Cup.	...	388
" " " c. Resorcin	...	752	" Eucainæ, 10%	...	344
" " Aconitinæ, 2%	...	100	" Eucalypti et Ac. Bor.	...	615
" " Agotan Co.	...	318	" Ferri Persulph.	...	421
" " Adamson (Ringworm)	...	1093	" Fuchsin	...	320
" " Adrenalin	...	982	" Galeni	...	876
" " Allantoin	...	890	" Galloë, 1 in 5	...	359
" " Allyl Sulphid.	...	838	" " c. Opio (7.5%)	...	631
" " Amyl Salicyl Co.	...	73	" Guaiacol	...	446
" " Anderson	...	231	" Gynocardia	...	607
" " Antimonii	...	168	" Hamam.	...	449
" " Aquæ Rosæ	...	876	" Hydrarg.	456, 83	
" " Argenti Nitratis Co.	...	175	" Hydrarg. Dil.	456, 457	
" " Argyrol	...	176	" " Ammon. (and Dil.)	...	458
" " Aristol	...	510	" " Co., 2 in 5	...	457
" " Atropinæ, $\frac{1}{2}$, 1 and 2%	...	215	" " et Pot. Iodid.	...	465
(latter B.P. '14)	...	215	" " et Zinci Cy., 1 or 2%	...	482
" " c. Acid Boric	...	215	" " Iodidi Rub.	...	463
" " c. Cocaina	...	215	" " Mite	456, 457	
" " Bals Peruv.	...	843	" " Nitrat., and Dil.	466, 83	
" " Bazin's	...	476	" " Oleatis, 602; Co.	...	602
" " Belladonnæ	...	237	" " Or. Flavi	...	476
" " B. Naphthol Co.	...	571	" " " c. Atrop.	...	215
" " Betulæ Co.	...	704	" " " c. Physostig.	...	694
" " Billrothi	...	175	" " " Rubri	...	477
" " Bismuth Co.	...	232	" " et Canth.	269, 477	
" " " Morph. et Cocain	...	228	" " Salicyl-Arsenas	...	458
" " Bismuthi Oxychl.	...	232	" " Subchlor.	...	475
" " " Subgall.	...	237	" " c. Morph., L.I.P.	...	475
" " Brilliant Green	...	325	" " Sulph. Flav.	...	477
			" " Hydrog. Peroxid.	...	495
			" " Hyoscina	...	498
			" " Ichthosulphol et Rosatum	...	504

FIGURES IN HEAVY TYPE, e.g. 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
<i>Ung. Iodi</i> , 1 in 25 ...		516	<i>Ung. Simplex</i> ...		815
„ „ <i>Intinctum</i> .		516	„ <i>Sod. Chlorid.</i> ...		770
„ „ <i>Iodoformi</i> .		509	„ <i>Sodii Perboratis</i> ...		13
„ „ c. <i>Atrop.</i> ...		215	„ <i>Sodii Perox.</i> ...		496
„ „ c. <i>Eucalypto</i> ...		509	„ <i>Staphisagrie</i> ...		888
„ <i>Iodolysin</i> .		766	„ <i>Stimulans</i> ...		269
„ <i>Iohydrin</i> , 25% ...		522	„ <i>Stovain c. Adrenalin</i> ...		353
„ <i>Ipecac. et Crotonis</i> ...		525	„ <i>Styracis</i> ...		888
„ <i>Kaolin</i> ...		144	„ <i>Sulph. Camphorat</i> ...		798
„ <i>Kaposi</i> ...		571	„ <i>Sulph.</i> , 798; c. <i>Hyd.</i> ...		798
„ <i>Lanæ Hydros</i> ...		101	„ <i>Sulph. Hypochlor.</i> ...		798
„ <i>Lanæ Comp.</i> ...		101	„ „ <i>Iodidi</i> ...		798
„ <i>Lano-boric Camph.</i> ...		11	„ „ <i>Naphthol Salicyl.</i> ...		798
„ <i>Menthol c. Camph.</i> ...		557	„ „ <i>Zinc. et Kaolin</i> ...		798
„ <i>Mercurom</i> ...		480	„ <i>Suprarenal.</i> ...		976
„ <i>Metallorum</i> ...		466	„ <i>Thiosinamin</i> ...		765
„ <i>Methyl Salicyl Co.</i> ...		72	„ „ <i>et Antipyrin</i> ...		765
„ <i>Myrobalani</i> , also c. <i>Opio</i> ...		855	„ <i>Thorii Oleatis</i> ...		809
„ <i>Naphthol Co.</i> ...		571	„ <i>Thymol (& Co.)</i> ...		812
„ <i>Neapolitanum</i> ...		456	„ <i>Tuberculin Philip's</i> ...		947
„ <i>Neisser-Siebert</i> .		471	„ <i>Tuberculin Kochi</i> ...		937
„ <i>Oleatorum</i> ...		604	„ <i>Uranii Oleat</i> ...		604
„ <i>Olei Cadini et c. Sulph.</i> ...		704	„ <i>Veratrinæ</i> , 2% ...		893
„ <i>Ol. Cedri Atlant</i> .		849	„ <i>Viride</i> ...		884
„ <i>Ol. Ricini Co.</i> ...		621	„ <i>Whitfield</i> .		67
„ <i>Opil</i> ...		631	„ <i>Wilkinson</i> .		798
„ <i>Optochin</i> ...		388	„ <i>Wilsoni</i> ...		828
„ <i>Paraffini</i> .		654	„ <i>Zinci</i> , 15% ...		828
„ <i>Pagenstecher</i> ...		476	„ „ c. <i>Acid Salicyl.</i> ...		828
„ <i>Para-monochlor-phenol</i> .		21	„ „ <i>Carbol.</i> ...		828
„ <i>Pheno-boric</i> ...		11	„ „ <i>Oleatis</i> ...		603
„ <i>Physostigminæ</i> ...		693	„ „ <i>Permang.</i> ...		556
„ <i>Picis Liq.</i>		704	„ „ <i>Peroxidi</i> ...		496
„ „ <i>Co.</i> ...		704	„ „ <i>Unicorn Root, False</i> ...		862
„ „ <i>et Acidi Salicyl</i> ...		299	„ <i>Universal Indicator</i> ...		190
„ <i>Pilocarpinæ</i> ...		696	„ <i>University Cream</i> ...		597
„ <i>Plumbi Carb.</i> ...		707	„ <i>Unna's Chaulmoogra Pill</i> ...		609
„ „ c. <i>Calamina</i> .		830	„ „ <i>Jelly</i> , 813; <i>Paste</i> ...		829
„ „ <i>Iodidi</i> ...		707	„ „ <i>Salve Soap</i> ...		870
„ <i>Plumbi Oleatis</i> .		603	„ „ <i>Stain</i> ...		549
„ „ <i>Subacetatis</i> ...		706	„ <i>Unoline</i> ...		892
„ <i>Populeum</i> .		227	„ <i>Uradal</i> , 5 to 10 gr. ...		820
„ <i>Potassæ Sulph.</i> ...		709	„ <i>Uræmia</i> ...		388
„ <i>Potassii Iodidi</i> , 1 in 10 ...		458	„ <i>Uranin</i> .		678
„ pro <i>eczema</i> ...		458	„ <i>Uranite</i> ...		355
„ <i>Prophylaxis</i> ...	458, 474,	82	„ <i>Uranium</i> ...	323 et seq.	355, 356
„ <i>Quininæ</i> (40%) ...		729	„ „ <i>Acetate</i> ...		355
„ <i>Quin. HCl. Carbam.</i> ...		732	„ „ <i>Calcium Phosphate</i> ...		355
„ <i>Ranunc. Ficaricæ</i> ...		881	„ „ <i>Copper Phosphate</i> ...		355
„ <i>Reclus</i> ...		329	„ „ <i>Minerals</i> ...	323,	356
„ <i>Resinæ</i> ...		381	„ „ <i>Mud</i> ...		350
„ <i>Resorcini</i> (and <i>Co.</i>) ...		752	„ „ <i>Nitrate</i> ...		356
„ „ c. <i>Ac. Salicyl</i> ...		752	„ „ „ <i>Antiseptic Power</i> ...		278
„ <i>Rubrum, N.H.W.</i> ...		477	„ „ <i>Oleate</i> ...	604,	356
„ „ c. <i>Canth.</i> ...		477	„ „ <i>Oxide</i> ...		356
„ <i>Rumicis</i> ...		883	„ „ <i>Quinine Chloride</i> ...		356
„ <i>Rusci Co.</i> .		705	„ „ and <i>Ra. Relation-</i>		
„ <i>Sabinæ</i> ...		883	„ „ „ <i>ship</i> ...	326,	355
„ <i>Salol c. Cocaina</i> ...		82	„ „ <i>Salicylate</i> ...		356
„ „ c. <i>Menthol</i> ...		82	„ „ <i>Series Table</i> ...	323,	329
„ <i>Salvas</i> ...		770	„ „ <i>Urari</i> , 1/20 to 1/2 gr. ...		853
„ <i>Sawyer</i> ...		525	„ <i>Urea</i> , 10 to 60 gr., or more ...	815,	246
„ <i>Scabies, Danish</i> .		799	„ „ <i>Estimation of</i> ...		387
„ <i>Scarlet</i> ...		313	„ „ <i>Concentration Test</i> ...	816,	385
„ <i>Sedresol</i> ...		705			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Urea Naphthol Compds. sym-			Urine Test Case	...	391
metrical	...	316	Urine, Bromine in,	...	85
„ Quinine, 5 to 15 gr.	...	731	Uritone, 5 to 15 gr.	...	450
„ „ local anaesthetic...	...	731	Urobilin...	...	365
„ Stibamine	...	168	Urodonal, 3 dr. <i>p.d.</i>	...	454
Urease	...	76, 383	Uro-Hexoids	...	453
Ureides	...	316, 202	Urohypertensine	...	408
Ureometers	...	387	Uropherin, 5 to 15 gr.	...	806
Urethane, 10 to 60 gr.	...	824, 246	Urotropine, 5 to 15 gr.	...	450
Urethral Bougies	...	244	Ursol	...	308
<i>Uryinea</i>	...	892	Urtica Dioica	...	34
„ Maritima	...	885	Uta	...	552
Urinary Antiseptics Internal	...	304	Uteramin	...	407
Urine, 357; Aceto-acetic Acid,			Uva Ursi	...	841
in, 359, 360; Acetone in, 359;			Uviol, Light	...	315
Acidity of, 359, 382, 390;			(See also Ultra-violet, Light).		
Acidosis, 361; Albumin Tests			Vaccination Act, 952; Lancets,		
for (see also devisers' names),			Shields	...	953
361-364; Alkalinity of, 358,			Encephalitis following	...	545
390; Albumoses in, 362, 364;			VACCINES	...	896
Amino-Acids in, 365; Am-			<i>Limit</i> doses are given. Care must be		
monia in, 382; B. Coli in, 81,			taken to distinguish <i>Prophylactic</i> and		
391, 533; Bacteriology of,			<i>Therapeutic Doses</i> . See p. 900.		
390; Bence-Jones Albumose,			„ Acne, 5 to 500 mill.	...	905
361, 384; Benzoyl-Glycocoll			„ Acne, 5 m., with Staph.		
in, 381; Bile Pigments and			100 m. increased	...	905
Salts in, 365; Blood in, 392;			„ Actinomyces	...	504
β -Oxybutyric Acid in, 359;			„ Anthrax	...	905
Calcium in, 404; Calculi in,			„ Anti-rabic	...	568
367; Casts, 368; Chemical			„ Anti-Typhoid	...	949
Deposits, 358; Chlorides in,			„ „ Pas de Calais		
368; Cholesterin in, 384;			Expts.	898, 950	
Creatinine in, 368, 374; Cys-			„ Anti-Typhoid-para-		
tin in, 367, 369; Dextrin in,			Typhoid	...	949
369; Diacetic Acid in, 359;			„ Anti-Typhoid-para-		
Diastatic Test, 387; Fibrin,			Typhoid-Cholera	...	949
368; Formaldehyde in, 370;			„ Asthma	...	906
Fungi for detecting Sugar,			„ Autochthonous	904, 909,	919
379; Globulins, 364; Glucose			„ B. Coli, 5 mill. incr.	...	914
in, 370; Glyccerin in, 380;			„ „ „ in rheum. Ar-		
Gonococcus in, 390; Hæmo-			thritus	...	915
lytic Action of in anæmia,			„ Bordet Gengou B.	...	956
397; Hæmotoporphyrin 367;			„ Bronchitis	...	907
Hippuric Acid in, 381;			„ Castellani's Tetra, etc.	...	949
Histidin, 365; Indican in,			„ Catarrh	...	907, <i>et seq.</i>
381; Indoxyl in, 381; Joulie's			„ Cerebro-Spinal Meningi-		
Ratios, 382; Lævulose in,			tis, 50 to 2000 mill.	...	909
379; Leucin in, 365; Lym-			„ Children Doses	...	901
phatic System, effect on, 517;			„ Cholera 500 to 2000 m.		
Microscop. Examn., 357;			(Proph.)	...	913
Nitrogen in, 381; Oxy Buty-			„ Coli, 5 mill., incr.	...	914
ric Acid, 359, 361; Pentose			„ Combined Cold 50 to		
in, 380; Peptones in, 364;			1000 mill.	...	908
Phosphates in, 382; Purins			„ Detoxicated	...	901, 923
in, 383; Pus in, 383; Quinine			„ Diphtheriæ 25 to 500		
Estn. in, 60; Renal Function			mill.	917
Tests, 384; Sp. Gr. of, 357,			„ Doses of, Table.	900, 902	
370, Sugar in, 370; Tubercle			„ „ Children...	...	901
Bacilli in, to stain, 391, 601;			„ Dysentery, 5 to 2000 mill.	...	918
Tyrosin in, 365; Urea in,			„ Friedlander B., 5 to		
estimation of, 384, 385, 387;			1000 mill.	...	908
Uric Acid in, estimation,			„ Glanders, 1 Cc.	...	547
389; Urobilin, etc., in, 365;					
Urostealith, 368; Volume					
<i>p.d.</i> , 357; Xanthin, 368.					

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Vaccines—<i>contd.</i>			VACCINES. SENSITIZED		901, 956
<i>Therapeutic Doses.</i>			„ B. Coli, Cereb. Sp.		
„ Gonococcus, 25 to 1000 mill. ...		918	Fever, Gono., Influenza, Pneumococcus, Staphylo., Alb. Aur. (and mixed), Strepto, and Typhosus		956
„ Hay Fever, 25 to 1000 units. ...		920	Vaccinia, 952 <i>et seq.</i>		
„ Hexa (Castellani) ...		949	Vaccinium Myrtillus ...		872
„ Immunising Power of. ...		902	Vaccinum ...		952
„ Influenza, 10 to 2000 mill. ...		921	Vacuum Vessels ...		141, 495
(<i>cf.</i> Combined Cold Vaccine 908.)			Vaginal Suppositories ...		431, 801
„ Influenza Detoxicated		923	Valenta figure ...		159
„ Local & General Effects		904	<i>Valerianæ Rhiz. (et Indic.)</i> ...		824
„ Lymph ...		952	Valerianic -iso-amyl-Ester ...		826
„ Malta Fever ...		560	Validol, 10 to 15 m. ...		558
„ Micrococcus Catarrhalis, 10 to 2000 mill. ...		908	Valkasa ...		38
„ Ozæna, 50 to 1000 mill. ...		923	Vanadate Test ...		14
„ Parodonta Strepto., 5 mill. increased ...		926	Vanadine, Vanadium ...		892
„ Penta (Castellani) ...		949	Van den Bergh Test ...		1053, 611
„ Peptone with ...		672	Van Ermengem's Stains ...		605
„ Per os. 898, 909, 919, ...		950	Vanilla ...		415
„ Plague... ...		563	Vanillin ...		892, 415
„ Pneumococcus, 10 to 2000 mill. (Prophyl., Wright, 924) ...		924	Van Swieten's Liquor ...		468
„ Pollen ...		919	Vapor Acidi Carbolici, 19; Ac. Carbol. Comp., 386; Allii Succ., 838; Ammon. Chlor., 146; Chlorof. Co., 386; Creosoti and Co., 385, 386; Cubebæ c. Limone, 853; Eucalpt. and Co., 615; Guaiacol Co., 446; Iodi Ætherealis, 516; Menthol Citriodor, 557; Terebeni, 803; Thymol ...		812
„ Preparation ...		901	Varalettes, 635; Varicella ...		996
„ Pulmonary Catarrh ...		907	Varicose Veins, Salicylate Injns (See also Therap. Index).		70
„ Pyorrhœa, 5 m. incr. ...		926	„ Quinine Urethane Injns... ..		741
„ Rabies ...		568	„ Ulcers ...		741, 1096
„ Refs., general ...		903	Variola, 952 <i>et seq.</i> ...		996
„ Renner's ...		953	Varium ...		964
„ Rheumatic 5 to 1000 m. ...		927	Varnishes, Micro ...		869 & 616
„ Scarlet Fever, 5 mill. incr. ...		929	Vaseline, Brand Petroleum Jelly (Oil or Liq., 655) ...		654
„ Septus B., 50 to 2000 mill. ...		908	„ High Meltg. ...		654
„ Site of Injection ...		904	„ Off. Fr. CX. ...		655
„ Standardisation ...		901	Vasoconstrictine ...		976
„ Staphylococcus, 100 mill. incr. ...		930	Vasodilatin ...		973
„ Streptococcus, 5 to 2000 ...		929	Vasodilators, 154, and see Therap. Ind.		
„ „ Conglomeratus ...		929	Vasopressin ...		966, 169
„ Streptococcal Parodontal 5 mill. increased ...		926	Vasotonin ...		976
„ „ Rheumaticus, 5 to 1000 mill. ...		927	Veal Peptones ...		582
„ 'T.A.B.' ...		949	Veedip Gloves ...		270, 261
„ Table of ...		900	Veg. Albumen, 591; Mercury... ..		707
„ Technique of Injection		904	Venereal, see Gonorrhœa and Syphilis ...		
„ Tetra (Castellani) ...		949	Venereal Diseases Act (1917)... ..		1022
„ Tubercle, 938; <i>see also</i> Tuberculin			„ Packets ...		82
„ Typh. <i>see</i> Vaccine Anti-typoid ...			„ prophylaxis 458, 461, 474, 82		
„ in rheum. arthritis		675	Venice Turps. ...		701
„ Varieties of ...		901	Veno's Cough Cure ...		636
„ War Office Conf. on Influenza ...		921	Veramon Tabs., 1 to 1½ ...		330
„ Whooping Cough, 5 to 2000 mill. ...		956	Veratri Virid. Rad., 1 to 5 gr....		893
„ „ „ Compound		956	Veratrina, 1/64th to 1/16th gr. 893, 246		
			Veratrinæ Oleatum ...		893

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Veratrole	893	Vin Digitale Comp.	398
Veratrone, 1 Cc.	893	„ Diuretic, $\frac{1}{4}$ to 1 oz.	865
Verbascum, 893; Verbena	875, 894		„ Emetinæ, 5 to 45 m.	531
Verdigris	389	„ Ergotæ, av. 2 dr.
Vermicides, <i>see</i> Hyd. Am-			„ Ferri, 2 dr.	415
mon. and Parasites (Ther. Ind.)			„ „ Amar., 2 dr.	415
Tetrachlorethane	293	„ „ Citratæ, 1 to 4 dr.
Trichlorethylene	293	„ „ Glyceroph., $\frac{1}{2}$ to 2 oz.	37
Vermijelli.	659	„ Ipecacuanhæ (10 to 30 m.
Vermilion	477	expt.), (4 to 6 dr. emetic)	525, 39	
Vermin Killers:—			„ Kola	253
Battle's and Butler's contain			„ Opii, 10 to 30 m.	631
Strychnine	„ „ Crocat., 5 to 20 m.	631
Hammond's and Simpson's			„ Pepsinæ, 1 to 2 dr.	663
contain Arsenic	„ Quininæ, 4 to 8 dr.	730
Vermouth	832	„ Quinquina Off. Fr. Cx.	297
Verne's Syph. Test	534	„ Rhei, '85, 1 to 2 dr.
Vernisol	425	„ Tann-Iodo-Phosph., $\frac{1}{2}$ to 2oz.	514	
Vernon Harcourt Regulator	...	285	„ Trousseau	398
Veronigen, 1 dr.	820	Vinolia Soap	761
Veronal, 5 to 10 gr. ...	817 & 68,	231	Viola var., 30 to 60 gr.	894
„ Dangers of	818, 819		Violet Gentian	321
„ Poisoning	818	„ „ Crystal	321, 324
„ Sodium, 5 to 10 gr.	819	Viper's Bugloss	855
Vervain	894	Virol	959 &	636
Vesalvine, 5 to 15 gr.	450	Viscose Silk	440,	443
„ 'B' (Benzoas 5 to 15 gr.)	452		Viscometer	143
„ Efferv., 1 dr.	452	Viscum Album	894
„ 'S' (Salicyl), 5 to 15 gr.	453		Visem	38
„ Antiseptic Power ...	273		Vita Glass	779,	318
VESCETTES	894	Vita Wheat	112
Carlsbad	780	Vitafer	37,	590
Lithium Cit., 3, 5 gr.	543	Vitali's Test	66,	215
„ Hipp., 5 gr.	543	Vitamins	592 &	98
Mag. Sulph., 30 gr.	548	„ Cod Liver Oil Concentrates	613	
Piperazine, 5 gr.	703	„ Distribution of 593, 594	98 et seq.	
Pot. Citrate	712	„ in Strawberries	858
Sodio-Mag. Sulph. etc. Caffeine	780		„ Destroyed by heat, etc. 593,	594	
Sod. Phosph., 50 gr.	777	(See also A.B.C., <i>infra</i>).		
Sod. Salicyl., 5 gr.	70	„ Commercial preps. ...	597, 102	
Stront. Brom., 10 gr.	789	Vitamin 'A'	593, 98,	99
Vesuvine	535	(anti-infective),		
Vespyrin, 15 gr.	82	Arsenic and Antim Tests ...	99	
Vet. Surgeon's Scrip for			„ 'B,' Destruction by heat		
Drugs	1004 and 1008		and oxidation	593, 102	
Vibron Septique	546, 559		„ Dual Nature of	102
Vibro Cholerae	913 & 439		„ Stability	101
Vibrona	636	„ in Spinach	100, 106	
Vibrona Malt (Bronamalt)	...	550	„ In Yeast and seed germs. ...	593,	103
Viburnum Prunif.	894	(See also Beri Beri, 505)		
Vichy Water	772 & 456,	458	Vitamin 'C,' 593, 97, 103; and		
Vienna Paste	709	Scurvy, 597, 103; Tablets,		
Vinca Major	894	Bassett Smith's (Antiscorb.)	593	
Vincent's Angina	1097	Destruction by heat... ..	593, 103	
„ Fusiform B.	926	in Germinating Seeds	593, 103	
Vinegar	in Milk destroyed	103
Vin Antimoniale, 10 to 30 m.,			in Orange juice	104
emetic, 2 to 4 dr.	166	in Tomatoes tinned	593
„ Aurantii	842, 26	Vitamin 'D,' 594, 97, 104; and		
„ Cascarae, $\frac{1}{2}$ to 1 oz.	279	Rickets, 594, 595 et seq.,	101, 104	
„ Chinæ, 1 to 4 dr.	297	Coward Unit...	105
„ Cocæ, 2 to 4 dr.	332	Jephcott Unit	105
„ Colchici, 10 to 30 m.	358	Caries in, <i>re</i>	105
„ Condurango, $\frac{1}{2}$ to 1 oz.	852			
„ de l'Hotel-Dieu	398			

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Vitamin 'D'— <i>contd.</i>			Water Iodine, Estimation Pal-		
Patent Rights ...		106	ladium Method		425
Rickets, Light in relation to		596, 104	" " " Permang. Me-		424
" Mercury Lamps in		596, 104	thod ...		424
Vitamin 'E' ...		594, 106	" " " Sodium Nitrite		424
" in Wheat Germ Oil		106	Method ...		424
Vitamogen ...		598	" " Finland ...		431
Vitellin, 176; Vitis alba		845	" " " significance of ...		423
Vitmar ...		598	" " Germany ...		431
Vlemingx's Solution		261	" " Goitre, associated		
Voice Tablets ...		711	with ...	426, 429	
Volckmann's Sol. ...		812	" " Hercus' work		429
Volhard Method ...		416	" " Heymann's work	426, 430	
Vollsalz ...		714	" " Holland ...		430
Volt ...		282	" " Llandudno... ..		427
Volumetric Indicators		187	" " London Artesian ...	429	
Von Heyden '471' ...		169	(See also Met. Water Board).		
Von Pirquet's Test ...		947	" " Manchester ...	427	
Vulpro Waterproof Sheetting		271	" " Met. Water Board		
Vuzin ...		388		425-427, 433	
Wagner's Reagent ...		205	" " " " Drought,		
Walker I. C., Tests ...		664	effect on	429	
Wallflower ...		850	" " Mineral ...		427
Walnut Hair Dye ...	308,	864	" " Nebraska ...		431
Wang Medium ...		620	" " New Zealand ...		429
Warburg's Tincture, 1 to 4 dr.		739	" " Norwich ...		427
Warner's Safe Cure ...		636	" " Oxford ...	427, 429	
Washing without Soap ...		762	" " Plymouth ...		427
Wassermann's Reaction ...		579	" " Rowett Research In-		
WATER ANALYSIS, 418; Hor-			stitute Work	423, 426,	
rock's Method		434		429	
" " Bacteriological		435 <i>et seq.</i>	" " Sea ...		428
" " " and Chem.			" " Spa Waters ...		427
compared		443	" " Von Fellenberg's		
" Antibacterial Action of			work on	426, 428, 430	
Rhone ...		443	" Lead in ...		421
" Board Reports ...		440-443	" London, Magnesium in...		421
" Chlorination ...	45, 715,	432	" Metals in ...		420
" Cress ...	872, 99,	166	" Mineral ...		447
" Distilled, Bact. Examn...		435	" Non-electrolyte ...		285
" " H Ion Concentn...		192	" Peaty ...		421
" Dropwort...		875	" Pennywort ...		362
" Gas ...	142,	501	" Pepper ...		878
" Germander ...		890	" Poisons in ...		434
" Glass ...		778	" Radium in ...		350
" Helium in ...		337	" Sea, Iodine in ...		428
" Hemlock ...		851	" Softeners ...	761,	443
" IODINE IN, 715, 775, 918,		422	" Sterilising Tablets		779
<i>et seq.</i>			" " by Chlorine	45, 715,	432
" Adlercreutz's work.		431	" " Copper ...		433
" Canterbury ...		427	" " " Ozone ...		433
" Chlorination, effect			" " " Permanganate...		555
of, 428, 430, 431,			" " " Succin Chlorim		433
432; on Stego-			" " " Ultra-Violet Lgt.		433
myia ...		432	" " " Army (Alum)		434
" Conclusions ...		433	" Swimming Bath...		447
" Estimation, Modifd.			" Zinc in ...		421
Hunter's Mthd.		422	Waterproof Shtg. ...		271
" Isabella Leitch			Watkins' Test ...		560
and J. M.			Wattle Bark = <i>Acac. Decurrens</i>		832
Henderson		423	Wave Lengths ...	316,	340
" Oxygen Incin.			Wax, Bees, 849; Dental, 655;		
Method.		425	Carnauba ...		248
			Wax, Horsley's ...		849
			" Paraffin ...		653

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Waxes, M.Pts. of	243	469, 471; Pioric, 63; Salicyl,	...	413
Webster's Test	61	67; Styptic	422, 759, 1098
Weed Killers	35	Worms	759
Weights and Measures...	xxxviii		Wormseed (Levant)	832
„ Atomic	xxxviii	Wormwood	164
Weil Felix Reaction	610	Wortabel Treatment	634
Weil's Disease	610	Woulf's Bottle for Oxygen	898
Wesson Oil	263	Wound Sucking	1099
Westoran, Westron	293	Wound Treatment	853
Westropol	293	Wourara, 1/20th to ½ gr.	...	437
Westrosol	292	Wrappers, Surgical	862
West's Swab	911	Wrightia Antidys.	299, 761
Whale Oil	100	Wright's Coal Tar Preps.	...	396
Whatmough's Iodine Ampoules	...	518	„ Diluting Fluid	768
Whcat and Germ 107, Oil	106	„ Hypertonic Saline	567
„ Starch	839	„ Leishman Stain 397, Pipette,	...	774
Whey Powder	588	„ Pneumo.Culture Med.	...	759
Whiskey...	118, 26	„ Sod. Cit. Solution	
White Precipitate	458	Wurmsamen	
Whitehead's Varnish	508			
Whitfield's Ointment	67	Xanthaline	139
Whooping Cough, 1098; Bacil-	...		Xanthine	249
lus, 612; Infective Period,	...		Xanthoxylum <i>var.</i>	894
996; Vaccine	956	Xeroform, 5 to 20 gr., and Gauze	...	20
Whortleberry	872	X.L. All Fumigators	875
Widal's Reaction	603	“X” Rays, 291; Acne, 301;	...	
Wijs' Solution	87	Angina, 301; Arthritis Diag-	...	
Wild, Prof. Absorption of	...		nosis, 299; Barium Meals,	...	
Chemicals	87	222, 294; Bismuth Meals,	...	
Wilkinson on Tub. Treatment	...	944	228, 232, 294, 298; Blood	...	
Wilkinson's Ointment	798	Affections, 301; Bougies for,	...	
Willemite	333	294; Bronchial Asthma, 302;	...	
Willcox, Sir Wm. on Stomach	...		Bulbs, 292; Burns, 309;	...	
Examination...	415	Calculi Diagnosis, 297; Can-	...	
Williams' Pink Pills	637	cer Treatment, 304 <i>et</i> 306;	...	
Willmore on Dysentery	533,	537	Cathode and Anticathode,	...	
Willow, Black or Pussy	883	291; Catheters for, 294;	...	
Willowcine	892	Cinematography, 294; Coils,	...	
Wilson's Ointment (P. Jap.)	828	291; Color Sensitive Plates,	...	
Wilson's Erasmus—Hair Lotion	...		294; Coolidge Tube, 292;	...	
and Oint.	149, 269	Dangerous effects to opera-	...	
Wincarnis	627	tors, 309; ‘Deep’ Therapy,	...	
Windolite.	779	306; Dental use, 299; Derm-	...	
Wines	26	matitis, 309; Developers,	...	
Wingrave's Stain	400	296; Diagnosis, 296; Dos-	...	
Winslow's Syrup	637	age, 306; Duplitized Films,	...	
Wintergreen Oil, 5 to 15 m.	72	293; Eczema treated, 302;	...	
Wireless Headphone Death	312	Erlangen Treatment, 306;	...	
Witch Hazel	448	Exophthalmic Goitre treated,	...	
Witte's Peptone	669	302; Films, 293; Frankfurt	...	
Wolfram...	315	Treatment, 306; Gall bladder,	...	
Wooldridge's Tincture...	637	ex., 681; Gas Tubes, 292;	...	
Wooldridge, Prof. G. H., on Milk	...	483	Gastric Ulcer Diagnosis, 298;	...	
Wonderberry	887	Gynæcology, 303, 305; Hard	...	
Wood Naphtha...	119	Tubes, 293; Holzknecht	...	
„ Oil, ½–2 dr., 843; Sorrel	...	167	Scale, 307; Hyperidrosis,	...	
„ Spirit, 119; Poisoning	119	303; Industrial use, 310;	...	
„ Wool Perchlor.	469	Internat. Cong. Stockholm,	...	
Woodward's Gripe Water	637	306; Iodo-Ray with, 679;	...	
Wool Absorbent, 437; Animal,	...		Ionising Effects to operators,	...	
436; Blue, 472; Carbolic, 16;	...		309; Interpretation of Nega-	...	
Camphor, 264; Cyanide, 462;	...		tives, 297; Kienbock Quanti-	...	
Fat, 100; Lamb's 436;	...		meter, 307; Lead Shields,	...	
Mercuric Iodide, 463; Non-	...		295; Leukæmia, 301; Local-	...	
Absorbent, 437; Perchloride,	...		izer, Cross Thread, 297;	...	

FIGURES IN HEAVY TYPE, *e.g.* 100, REFER TO VOL. II.

NAME.	DOSE.	PAGE	NAME.	DOSE.	PAGE
Lupus, for, 303; Malignant Disease, 304; Meals, 222, 228, 232, 294; Measurements of Current, 307; Metal, Wood, etc., Examn., 310; Metalix Tubes, 292; Moles, 305; Nævi, 305; Opaque Substances, 292; Paraffin Wax, 308; Printing Paper, 294; Protection Com. Report, 309; Pruritus, 305; Psoriasis, 305; Pyelography, 297; Ringworm Treatment, 305; Rodent Ulcer Treatment, 305; 'Rontgen' 306; Sabouraud's Pastelles, 307; Screens, 292; Secondary Radiation, 295; Shields, 295, 296; Silhouette Radiographs, 294; Silk, 296; Skiagraphs, 297; Skin Affections, 305; Sodium Brom. and Iod. Sols., 297; Soft Tubes, 293; Stomach Examn., 298, 418; Teeth Examn., 299; Telephone Probe, 297; Thorium Pyelog. Medium, 298; Treatment, 301 <i>et seq.</i> ; Tubes, 291 <i>et seq.</i> ; Unit ('Rontgen') 306; Urinary Tract Examn., 771, 297; Wax, 308; Wehnelt Radiometer, 307; Whooping Cough treated ... 306			Zambeletti's Iron & Arsenic Drops, 5 drops ... 183		
Xylene, 312; Xylenols, Antiseptic pr., 279; Xylonite, 361; Xylol, 312; Xylol Balsam ... 162			„ Injections, 5 to 10 m. ... 183		
Xylol-azo-Xylol-azo-β Naph. Sulph.... ... 314			Zea Mays. ... 839		
Yadil ... 131			Zedoary ... 739		
Yagé ... 894			Zenker's Fluid ... 616		
Yatren ... 319, 538			Ziehl-Neelsen's Stain ... 598		
„ Casein ... 320			Zinc Arsenic Free ... 826		
Young's Dose Table ... 1108			„ & Starch Powders ... 829		
Yaws ... 192, 197, 241, 1099 & 612			„ Chloride Solution ... 827, 999		
Yeast, ½ to 1 oz., Extracts, 279, 98; Tests ... 378			„ Cream ... 828		
„ Vitamin 'B' in 593, 506, 507			„ Ionisation ... 289, 290		
Yellow, Aniline 497; Fever ... 612			„ Pastes, Various ... 829		
„ Ointment ... 476			„ Points ... 831		
Yeoman Flour ... 112			Zinci Acetas, 1 to 2 gr. ... 827		
Yeo's Mist. Anti-Catarrh., 1½ ozs. 149			„ Benzoas ... 827		
„ Chloric. Quin., 1 oz. 737			„ Bromid., 2 to 5 gr. ... 827		
Yerba (Maté) ... 253			„ Carbonas ... 827, 829		
„ Santa ... 894			„ Chloridum ... 827, 278		
Yersin's Serum ... 563			„ „ Aniline ... 278		
Yew ... 820			„ Citras, 3 to 12 gr. ... 828		
Yoghourt (See Curdled Milk) 58 & 40			„ Cyanidum ... 828		
Yohimbine, 1/20 to 3/20 gr. 895, 246			„ et Hyd. Cyanid. ... 461		
Yohimba var. ... 895			„ Gelatin ... 829		
Yperite ... 1102			„ Ichthosulphol ... 504		
Zam Buk ... 637			„ Iodas ... 834		
			„ Iodidum, av. 1 gr. ... 828		
			„ „ Ionisation ... 290		
			„ Lactas, ¼ to 3 gr. ... 828		
			„ Margosas ... 843		
			„ Oleas ... 603		
			„ Oleo-Stearas ... 603		
			„ Oridum, 3 to 10 gr. ... 828		
			„ Oxychlor. ... 830		
			„ Oxyphosph. ... 830		
			„ Oxysulph. ... 830		
			„ Permang. ... 555 & 278		
			„ Peroxid. ... 496		
			„ Phenol-para-sulphonas ... 19		
			„ Phosphid., 1/20 to 1/3 gr. 690		
			„ et Potass. Cy., ½ to 1 gr. 828		
			„ Salicyl., 1 to 5 gr. ... 830		
			„ Silicas (= Willemite) ... 333		
			„ Stearas ... 604		
			„ Sulphanilas ... 309, 278		
			„ Sulphas., 1 to 3 gr. tonic, 10 to 30 gr. emetic, 831; Antiseptic Power, 278; Spray in C.S. ... 831		
			„ Fever ... 831		
			„ Sulphate Uterine Points ... 332		
			„ Sulphide "Active" ... 246, 278		
			„ Sulphocarbolas ... 19, 246, 278		
			„ Sulpho-ichthyolat ... 504		
			„ Tannas ... 96		
			Zinc Valerianas, 1 to 3 gr. ... 826		
			Zingiber, 5 to 15 gr. ... 895		
			Zirconia ... 58		
			Zittmann's Decoctions ... 884		
			Zoe Antiseptic ... 13		
			Zotak ... 264		
			Zotak ... 637		
			Zotak ... 646 & 76		
			Zymase ... 13		
			Zymocide ... 13		

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